# STIC Search Report
## Biotech-Chem Library

STIC Database Tracking Number: 113939

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|---|---|
| **To:** Ganapathy Krishnan | **From:** Beverly Shears |
| **Location:** REM/5C18/5C25 | **Location:** Remsen Bldg. RM 1A54 |
| **Art Unit:** 1623 | **Phone:** 571-272-2528 |
| **Friday, February 13, 2004** | beverly.shears@uspto.gov |
| **Case Serial Number:** 10/616278 | |

## Search Notes

Krishnan
10/616278



```
     FILE 'REGISTRY' ENTERED AT 08:43:20 ON 13 FEB 2004
                  E HYALURONIC ACID/CN 5
L1              1 S E3
                  E HEXOSAMINE/CN 5
                  E HEXOSAMINES/CN 5
L2              1 S E3
                  E GLUCOSAMINE/CN 5
L3              1 S E3
                  E "N-ACETYL-D-GLUCOSAMINE"/CN 5
L4              1 S E3
                  E "N-ACETYL-D-GALACTOSAMINE"/CN 5
L5              1 S E3
                  E HEXOSE/CN 5
L6              2 S E3
                  E CHONDROITIN SULFATE/CN 5
L7              3 S E3 OR E5 OR E22
L8              9 S L2 OR L3 OR L4 OR L5 OR L6 OR L7

     FILE 'HCAPLUS' ENTERED AT 08:44:52 ON 13 FEB 2004
L1              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HYALURONIC ACID"/CN
L2              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  HEXOSAMINES/CN
L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  GLUCOSAMINE/CN
L4              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-ACETYL-D-GLUCOSAMINE/
                  CN
L5              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-ACETYL-D-GALACTOSAMIN
                  E/CN
L6              2 SEA FILE=REGISTRY ABB=ON  PLU=ON  HEXOSE/CN
L7              3 SEA FILE=REGISTRY ABB=ON  PLU=ON  "CHONDROITIN SULFATE"/C
                  N OR "CHONDROITIN SULFATE A"/CN OR "CHONDROITIN SULFATE
                  C"/CN
L8              9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3 OR L4 OR L5
                  OR L6 OR L7
L9          15273 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR HYALURONIC OR
                  HYALURONAN OR HA(3A)HYALURON?
L10          5226 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (L8 OR HEXOSAMINE
                   OR GLUCOSAMINE OR CHONDROITIN(1W)(SULFATE OR SULPHATE
                  OR SO##) OR N(W)(ACETYL OR AC)(1W)(GLUCOSAMINE OR
                  GALACTOSAMINE OR GAL) OR ACETYLGLUCOSAMINE OR ACETYLGALAC
                  TOSAMINE OR HEXOSE)
L11            70 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND (LUBRICANT OR
                  LUBRICAT?(3A)AGENT OR MOISTURIZ? OR MOISTURIS? OR
                  NUTRACEUT?)
L12             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (OSTEOARTHRIT?
                  OR (OSTEO OR DEGENERAT?)(3A)(ARTHRIT? OR ARTHROSIS) OR
                  OSTEOARTHROSIS OR ANTIOSTEOARTHR? OR DEGENERAT?(3A)(JOINT
                  (W)(DISEAS? OR DISORDER)))

L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:397930  HCAPLUS
DOCUMENT NUMBER:          136:374807
TITLE:                    Cosmetic or pharmaceutical composition based on
                          lipoic acid and pyruvic acid
INVENTOR(S):              Gianfranco de Paoli, Ambrosi
PATENT ASSIGNEE(S):       General Topics S.R.L., Italy
SOURCE:                   Ital., 20 pp.
                          CODEN: ITXXBY
DOCUMENT TYPE:            Patent
LANGUAGE:                 Italian
```

Searcher : Shears 571-272-2528

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| IT 1299623 | B1 | 20000324 | IT 1998-BS10 | 19980223 |

PRIORITY APPLN. INFO.: IT 1998-BS10 19980223

AB The invention concerns a composition for cosmetic or pharmaceutical use which contains as active ingredients at least lipoic acid (both reduced form and dehydrolipoic acid) and pyruvic acid, their salts, esters, and amides and stereoisomers. Each may be present in amts. from 0.0001 to 90% weight/weight

IT **3416-24-8, Glucosamine 7512-17-6, Acetylglucosamine 9004-61-9, Hyaluronic** acid
RL: COS (Cosmetic use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cosmetic or pharmaceutical composition based on lipoic acid and pyruvic acid)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 08:49:29 ON 13 FEB 2004)
L13 9 S L12
L14 9 DUP REM L13 (0 DUPLICATES REMOVED)

L14 ANSWER 1 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004053655 EMBASE
TITLE: Use of **nutraceuticals** and chondroprotectants in **osteoarthritic** dogs and cats.
AUTHOR: Beale B.S.
CORPORATE SOURCE: B.S. Beale, 1111 West Loop South, Houston, TX 77027, United States. drbeale@gcvs.com
SOURCE: Veterinary Clinics of North America - Small Animal Practice, (2004) 34/1 (271-289).
Refs: 68
ISSN: 0195-5616 CODEN: VCNAA6
PUBLISHER IDENT.: S 0195-5616(03)00132-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English

L14 ANSWER 2 OF 9 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-877188 [81] WPIDS
DOC. NO. CPI: C2003-247748
TITLE: New indol-2-ones useful for treating e.g. inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma.
DERWENT CLASS: B02
INVENTOR(S): BRONK, B S; CROSSON, R M; DEMELLO, K L
PATENT ASSIGNEE(S): (PFIZ) PFIZER INC; (PFIZ) PFIZER PROD INC

COUNTRY COUNT: 100
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003089427 | A1 | 20031030 | (200381)* | EN | 26 |

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

US 2003207897 A1 20031106 (200382)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003089427 | A1 | WO 2003-IB1339 | 20030410 |
| US 2003207897 | A1 Provisional | US 2002-374372P | 20020422 |
| | | US 2003-414856 | 20030416 |

PRIORITY APPLN. INFO: US 2002-374372P 20020422; US 2003-414856 20030416

AN 2003-877188 [81] WPIDS

AB WO2003089427 A UPAB: 20031216

NOVELTY - New Indol-2-one derivatives (I).

DETAILED DESCRIPTION - New Indol-2-one derivatives of formula (I) and their salts.

X and Y = H, halo, -NO2, T, -CF3, 3-8C cycloalkyl, T-O-, T-S-, T-SO-, T-SO2-, T-(C=O)-, 8-10C aryl-(C=O)-, 1-10C heteroaryl-(C=O)-, 1-10C heterocyclyl-(C=O)-, T-NH-(C=O)-, 8-10C aryl-NH-(C=O)- or (T)2-N-SO2;

T = 1-6C alkyl;

n = 0 - 2;

Q = 6 membered heterocyclic divalent radical of pyran, piperidine, 1,4-dioxane, morpholine, dithiane, thiomorpholine, pyridazine, piperazine, pyridine, pyrimidine, pyrazine, 1,3,5-triazine or 1,3,5-trithiane;

R1 = H, halo or T; and

R2 = T or 3-8C cycloalkyl.

ACTIVITY - Antiinflammatory; Analgesic; Osteopathic; Antiarthritic; Antirheumatic; Antigout; Dermatological; Immunosuppressive; Antipyretic; Virucide; Gynecological; Gastrointestinal-Gen.; Respiratory-Gen.; Antiasthmatic; Nootropic; Neuroprotective; Immunomodulator; Antiallergic; Cytostatic; Antianemic; Antiulcer; Anticoagulant; Vasotropic; Antiarteriosclerotic; Cardiovascular-Gen.; Cardiant; Cerebroprotective; Vulnerary; Anticonvulsant; Antiparkinsonian; Antimigraine; Antidepressant; Ophthalmological; Antipsoriatic; Muscular-Gen.; Antidiabetic; Nephrotropic; Anti-HIV; Antibacterial; Tocolytic; Hemostatic; Antithyroid; Antimalarial; Protozoacide.

MECHANISM OF ACTION - Cyclooxygenase-2 (COX-2) inhibitor.

An in vivo inhibitory potency of indol-2-one derivative (A1) against COX-1 and COX-2 activity was evaluated using an ex vivo

procedure on canine whole blood. Three canines were dosed with (A1) (5 mg/kg) orally in 0.5% methylcellulose vehicle and three canines were untreated. The zero-hour blood samples were collected followed by 2 hour post-dose blood sample collection. Test tubes were prepared containing 2 micro l either (A) calcium ionophore A23187 giving a 50 micro M final concentration, which stimulated the production of thromboxine B2 (TXB2) for COX-1 activity determination; or of (B) lipopolysaccharide (LPS) giving 10 nu g/ml final concentration, which stimulated the production of prostaglandin E2 (PGE2) for COX-2 activity determination. The sample of blood (500 micro l) was added to both test tubes, which were then incubated at 37 deg. C for one hour. After incubation, EDTA (10 micro l) was added, centrifuged at 4 deg. C and percentage inhibition was calculated after the work up. % Inhibition for COX-1 and COX-2 after 2 hours was 7 and 77 respectively. Thus compounds possessed good COX-2 selectivity.

USE - For treating an inflammatory disease or condition in a mammal including human, feline or canine, or pain associated with the inflammatory condition; for treating **osteoarthritis** and for joint treatment (claimed). The diseases include and pain associated with surgery or trauma, **arthritis** (including **degenerative joint disease,** spondyloarthropathies, gouty arthritis, systemic lupus erythematosus, juvenile arthritis and rheumatoid arthritis), fever (including rheumatic fever and fever associated with influenza and other viral infections), common cold, dysmenorrhea, menstrual cramps, inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, bronchitis, chronic obstructive pulmonary diseases, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer (such as solid tumor cancer including colon cancer, breast cancer, lung cancer and prostrate cancer; hematopoietic malignancies including leukemias and lymphomas; Hodgkin's disease; aplastic anemia, skin cancer and familial adenomatous polyptosis), tissue ulceration, peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis, recurrent gastrointestinal lesion, gastrointestinal bleeding, coagulation, anemia, synovitis, gout, ankylosing spondylitis, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joint implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic aneurysm and brain aortic aneurysm), periarteritis nodosa, congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neuralgia, neuro-degenerative disorders (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain (including low back and neck pain, headache and toothache), gingivitis, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, conjunctivitis, abnormal wound healing, muscle or joint sprains or strains, tendonitis, skin disorders (such as psoriasis, eczema, scleroderma and dermatitis), myasthenia gravis, polymyositis, myositis, bursitis, burns, diabetes (including types I and II diabetes, diabetic retinopathy, neuropathy and nephropathy), tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, immunodeficiency diseases (such as AIDS in humans and

FLV, FIV in felines), sepsis, premature labor, hypoprothrombinemia, hemophilia, thyroiditis, sarcoidosis, Behcet's syndrome, hypersensitivity, kidney disease, Rickettsial infections (such as Lyme disease, Erlichiosis), Protozoan diseases (such as malaria, giardia, coccidia), reproductive disorders (preferably in livestock) and septic shock (preferably arthritis, fever, common cold, pain and cancer).

ADVANTAGE - The compounds selectively inhibit cyclooxygenase-2. Dwg.0/0

L14 ANSWER 3 OF 9 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-598218 [56] WPIDS
DOC. NO. CPI: C2003-162295
TITLE: Modulating release of monosaccharides in humans or animals by delaying delivery of chondroprotective and chondrosynthesis stimulating agents, useful for treating **osteoarthritis**, Crohn's disease and ulcerative colitis.
DERWENT CLASS: B04 D16
INVENTOR(S): BOUCHER, I; BRUNET, S
PATENT ASSIGNEE(S): (ISMB-N) ISM BIOPOLYMER INC
COUNTRY COUNT: 102
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003054208 | A2 | 20030703 | (200356)* | EN | 26 |

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003054208 | A2 | WO 2002-CA1917 | 20021212 |

PRIORITY APPLN. INFO: US 2001-339339P 20011213
AN 2003-598218 [56] WPIDS
AB WO2003054208 A UPAB: 20030903
NOVELTY - Modulating release of monosaccharides in a human or an animal comprising treating a source of polysaccharides to produce oligosaccharides of desired length, administering at least one of the oligomers or its modified form to a human or animal to allow a lasting release of the monosaccharides and obtain a physiological effect, is new.

DETAILED DESCRIPTION - Modulating release of monosaccharides in a human or an animal comprising treating a source of polysaccharides to produce oligomers of saccharides of desired length, administering at least one of the oligomers or its chemically, biochemically or biologically modified form to a human or animal to allow a lasting release of the monosaccharides and obtain a physiological effect, where the lasting release lasts for a period of time proportional to

the length of the oligomers, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising an oligomer of saccharides modulating the release of monosaccharides having physiological effect selected from chondroregenerative or a chondroprotective effect, a prebiotic effect, a probiotic effect, a food additive effect, a **nutraceutical** effect, a wounding effect, an immunomodulatory effect, a systemic anti-inflammatory effect, a bacteriostatic effect, an anti-fungic effect or an antioxidant effect, in association with a pharmaceutical or **nutraceutical** carrier; and

(2) a prodrug for modulating the in vivo release of a monosaccharide consisting of an oligomer of saccharides units consisting of 2-100 or 2-25 monosaccharides.

ACTIVITY - Osteopathic; Antiarthritic; Antiinflammatory; Antiulcer.

A total of 9 beagle dogs were used to study the pharmacokinetic profile of the present invention. The results showed that administration by intravenous injection of a **glucosamine** formulation increased the ALP, which is indicative of cartilage or bone formation.

MECHANISM OF ACTION - **Glucosamine**-Modulator.

USE - The oligomer of saccharides is useful in the manufacture of a medicament capable of modulated lasting release of a monosaccharide for the treatment of systemic inflammation, in particular **osteoarthritis** (claimed). Other diseases include Crohn's disease and ulcerative colitis.

Dwg.0/3

L14 ANSWER 4 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002076625 EMBASE
TITLE: Efficacy of chondroprotective agents.
AUTHOR: Frenkel S.; DiCesare P.E.
CORPORATE SOURCE: Dr. S. Frenkel, Musculoskeletal Research Center, Hospital for Joint Diseases, 301 East 17th Street, New York, NY 10003, United States. sally.frenkel@excite.com
SOURCE: Current Opinion in Orthopaedics, (2002) 13/1 (9-13). Refs: 41
ISSN: 1041-9918 CODEN: COORE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Chondroprotective agents are substances capable of preventing, delaying, or reversing cartilage lesions due to **osteoarthritis**. Typically, aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) have been prescribed for pain relief in OA; their use is, however, associated with significant gastrotoxicity, and does not prevent joint deterioration. COX-2 inhibitors, while having fewer side effects, have recently been linked to cardiovascular complications. In the past several years, there have been reports of chondroprotective effects, as well as amelioration of pain, following intraarticular injection of

**hyaluronic** acid derivatives or oral administration of the so-called **nutraceuticals**, **glucosamine** and **chondroitin sulfate**. Because no mechanism of action for these agents has been demonstrated and sample sizes in many clinical trials have been small, their use remains controversial. This review examines the most recent clinical studies of these therapeutic modalities. .COPYRGT. 2002 Lippincott Williams & Wilkins, Inc.

L14 ANSWER 5 OF 9 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-194608 [25] WPIDS
DOC. NO. CPI: C2002-060094
TITLE: Composition for repairing connective tissues of animals e.g. in arthroses, **osteoarthritis** comprises exogenous hydrolyzed collagen, exogenous **glucosamine** and exogenous bioflavanol.
DERWENT CLASS: A96 B04 C06 G03
INVENTOR(S): BATH, T K; LYNCH, N
PATENT ASSIGNEE(S): (BATH-I) BATH T K; (LYNC-I) LYNCH N
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 6333304 | B1 | 20011225 | (200225)* | | 11 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 6333304 | B1 | US 1999-295001 | 19990420 |

PRIORITY APPLN. INFO: US 1999-295001 19990420
AN 2002-194608 [25] WPIDS
AB US 6333304 B UPAB: 20020418
NOVELTY - A composition comprises exogenous hydrolyzed collagen, exogenous **glucosamine** and exogenous bioflavanol.

ACTIVITY - Antirheumatic; antiarthritic; antiinflammatory.

MECHANISM OF ACTION - Chondrocytes stimulator; free radicals inhibitor.

USE - For repair of connective tissue in aged animals or animals with connective tissue injury such as a horse or other large animal, an adult human, dog or other medium sized animal and a cat or other small animals (claimed); e.g. suffering from arthritis, arthroses, **osteoarthritis** or traumatic injury.

ADVANTAGE - The composition supplement endogenous collagen stimulates chondrocytes for the production of collagen and cross-linking of collagen fibers with reduction in capillary leakage, inhibits mast cell degranulation, reduces histamine release, inhibits enzymes that break down collagen and elastin, scavengers free radicals and triggers the production of **hyaluronic** acids (**lubricants**), **chondroitin sulfate** (**glucosamine** glycans for holding and hydrating connective tissue and enzyme inhibition), keratan and proteoglycans (cartilage shock absorbers). The composition provides improved movement in the aged or injured animals in less than 4 weeks from initial ingestion.

Dwg.0/2

L14 ANSWER 6 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:9592 SCISEARCH
THE GENUINE ARTICLE: 267AB
TITLE: Therapeutic **nutraceutical** treatments for **osteoarthritis** and ischaemia
AUTHOR: Grant G F (Reprint); Gracy R W
CORPORATE SOURCE: UNIV N TEXAS, CTR HLTH SCI, OFFICE RES & BIOTECHNOL, ME 1-806, 3500 CAMP BOWIE BLVD, FT WORTH, TX 76107 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: EXPERT OPINION ON THERAPEUTIC PATENTS, (JAN 2000) Vol. 10, No. 1, pp. 39-48.
Publisher: ASHLEY PUBL LTD, 1ST FL, THE LIBRARY, 1 SHEPHERDS HILL HIGHGATE, LONDON N6 5QJ, ENGLAND.
ISSN: 1354-3776.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 72
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB There has been a very large increase in **nutraceutical** innovations, particularly in the US regulatory marketplace. This article reviews the therapeutic potential of a group of **nutraceuticals** that share common biochemical pathways, and have shown spectacular marketplace success. These are energy metabolites and precursor molecules involved in the metabolic mechanisms of cartilage replacement and cellular energy functions. The commercial **nutraceuticals** are **glucosamine**, ribose and their derivatives. These compounds are considered required nutrients for the repair of cartilage and connective tissues and optimal cellular energy maintenance in active, middle aged individuals. The recent scientific and patent literature in this segment of the **nutraceutical** marketplace is reviewed.

L14 ANSWER 7 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001019078 EMBASE
TITLE: Potential uses of velvet antler as **nutraceuticals**, functional and medical foods in the West.
AUTHOR: Sunwoo H.H.; Sim J.S.
CORPORATE SOURCE: Dr. J.S. Sim, Food Concept Antler Research Group, Dept. Agric., Food/Nutritional Sci., University of Alberta, Edmonton, Alta. T6G 2P5, Canada. jsim@afns.ualberta.ca
SOURCE: Journal of Nutraceuticals, Functional and Medical Foods, (2000) 2/3 (5-23).
Refs: 38
ISSN: 1089-4179 CODEN: JNFMFK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

Searcher : Shears 571-272-2528

AB Velvet antlers have been used as Oriental medicine for many centuries. Traditional medical reports and clinical observations from the Eastern world convincingly show that velvet antler is biologically active. However, little information is available on chemical and biological efficacy of antler products in the West due to the incomplete understanding of the uses and pharmacological properties of velvet antlers. To make antler products acceptable as **nutraceuticals** and functional foods in the West, antler research has been conducted to isolate and characterize the chemical and biological properties of velvet antlers. The chemical composition of antler was determined in four sections (tip, upper, middle, and base). Contents of dry matter, collagen, ash, calcium, phosphorus, and magnesium increased ($P < 0.05$), and those of protein and lipid decreased ($P < 0.05$) downward from the tip to the base. The concentrations of uronic acid, sulfated glycosaminoglycan (GAG), and sialic acid decreased ($P < 0.05$) downward. Amino acid and fatty acid contents, expressed as percentage of total protein and lipid, respectively, also varied ($P < 0.05$) among sections. The yield of **chondroitin sulfate** (CS) was approximately six fold greater in the cartilaginous (tip and upper) sections than in the bony (middle and base) sections. In addition to CS, the antler sections contained small amounts of keratan sulfate (KS), **hyaluronic** acid, and dermatan sulfate. Two proteoglycans associated with GAGs were also extracted from the cartilaginous section; a large aggregated proteoglycan with CS and KS and small molecules of decorin. Water soluble extracts rich in GAG stimulated the growth of bovine fibroblast in culture. Feeding antler diet for 54 days showed a significant effect on the growth rate of immunized rats. Diet antler powder resulted in a significant increase of HDL-C/LDL-C ratio ($P < 0.05$). The result appears to reflect the involvement of unknown factor(s) derived from the antler diet suggesting the importance for the prevention of the risk of coronary heart disease. Hematocrit value and iron content in plasma also significantly increased by feeding antler powder ($P < 0.05$). Thus, our data suggest that there are significant unknown factor(s) in the antler powder that enhances the biological performance of growing rats.

L14 ANSWER 8 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2000033966 EMBASE |
| TITLE: | Conservative management of the **osteoarthritic** knee. |
| AUTHOR: | Troum O.M.; Lemoine C. |
| CORPORATE SOURCE: | Dr. O.M. Troum, School of Medicine, University of Southern California, 2336 Santa Monica Boulevard, Santa Monica, CA 90404, United States |
| SOURCE: | Current Opinion in Orthopaedics, (2000) 11/1 (3-8). Refs: 41 ISSN: 1041-9918 CODEN: COORE |
| COUNTRY: | United States |
| DOCUMENT TYPE: | Journal; General Review |
| FILE SEGMENT: | 031 Arthritis and Rheumatism<br>033 Orthopedic Surgery<br>037 Drug Literature Index<br>038 Adverse Reactions Titles |
| LANGUAGE: | English |
| SUMMARY LANGUAGE: | English |

AB **Osteoarthritis** (OA) is the most common type of arthritis affecting synovial joints. Recent advances have altered the traditional progression of medical therapy for OA and have supplied new alternatives for the treatment of refractory OA. The new selective cyclooxygenase-2-inhibitory nonsteroidal anti-inflammatory drugs, celecoxib and rofecoxib, have significantly improved safety profiles, particularly with respect to serious gastrointestinal side effects and platelet inhibition. They should be used preferentially in higher-risk patients. Intra-articular viscosupplementation of the knee with exogenous **hyaluronic** acid **has** been approved by the US Food and Drug Administration as a medical device for the treatment of OA of the knee. It is reportedly as effective as nonsteroidal anti-inflammatory drugs for moderate OA of the knee. Finally, arthroscopic knee-joint lavage, with or without steroids, is another alternative for the treatment of knee OA; it should be considered before surgery is contemplated. Agents that may prevent cartilage degradation, such as the **nutraceuticals** ( **glucosamine** sulfate, **chondroitin sulfate** , and collagen hydrolysate) or inhibitors of nitric oxide or metalloproteinases, may prove beneficial but are still under investigation.

L14 ANSWER 9 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 94096368 EMBASE
DOCUMENT NUMBER: 1994096368
TITLE: **Hyaluronic** acid. A review of its pharmacology and use as a surgical aid in ophthalmology, and its therapeutic potential in joint disease and wound healing.
AUTHOR: Goa K.L.; Benfield P.
CORPORATE SOURCE: Adis International Limited, 41 Centorian Drive,Mairangi Bay, Auckland 10, New Zealand
SOURCE: Drugs, (1994) 47/3 (536-566).
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Hyaluronic** acid is a naturally occurring polysaccharide with distinct physicochemical properties which underlie its application as a viscoelastic tool in ophthalmological surgery. In cataract surgery the role of **hyaluronic** acid in facilitating procedures and protecting the corneal endothelium is well established. Some benefit was also been gained with the use of **hyaluronic** acid in penetrating keratoplasty trabeculectomy retinal reattachment and trauma surgery although its efficacy in these indications is less well-defined in the published literature. In addition to its lubricating and cushioning properties demonstration of some in vitro anti-inflammatory activity and a possible disease-modifying effect for **hyaluronic** acid in animals **has** prompted its investigation as a treatment in

**osteoarthritis** and to a much lesser extent in rheumatoid arthritis. **Hyaluronic** acid 20mg as weekly intra-articular injections for 3 to 7 weeks improved knee pain and joint motion in patients with **osteoarthritis**. Although this occurred to a greater degree than with placebo in most comparisons the effects of **hyaluronic** acid was similar to those of placebo in the largest trial. In the few available comparisons with other agents **hyaluronic** acid appeared equivalent to methylprednisolone 40mg (for 3 weeks) and to a single injection of triamcinolone 40mg. **Hyaluronic** acid was distinguished from other therapies by providing a sustained effect after treatment discontinuation. Together with its very good tolerability profile these properties justify further study of **hyaluronic** acid in patients with **osteoarthritis**. Some limited evidence of improvement in patients with rheumatoid arthritis and a possible healing effect of **hyaluronic** acid on tympanic membrane perforations represent additional areas of interest for future investigation. In summary **hyaluronic** acid is a well-established adjunct to cataract surgery and may prove to be a promising option in the treatment of patients with **osteoarthritis**. Its very good tolerability provides further impetus for examination of its potential role in on extended scope of arthritic and ophthalmological indications and in wound healing.

FILE 'HCAPLUS' ENTERED AT 08:51:29 ON 13 FEB 2004

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "HYALURONIC ACID"/CN

L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON HEXOSAMINES/CN

L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON GLUCOSAMINE/CN

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON N-ACETYL-D-GLUCOSAMINE/CN

L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON N-ACETYL-D-GALACTOSAMINE/CN

L6 2 SEA FILE=REGISTRY ABB=ON PLU=ON HEXOSE/CN

L7 3 SEA FILE=REGISTRY ABB=ON PLU=ON "CHONDROITIN SULFATE"/CN OR "CHONDROITIN SULFATE A"/CN OR "CHONDROITIN SULFATE C"/CN

L8 9 SEA FILE=REGISTRY ABB=ON PLU=ON L2 OR L3 OR L4 OR L5 OR L6 OR L7

L9 15273 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HYALURONAN OR HA(3A)HYALURON?

L15 123 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND ((OSTEOARTHRIT? OR (OSTEO OR DEGENERAT?)(3A)(ARTHRIT? OR ARTHROSIS) OR OSTEOARTHROSIS OR DEGENERAT?(3A)(JOINT(W)(DISEAS? OR DISORDER)))(S)(TREAT? OR THERAP? OR PREVENT?) OR ANTIOSTEOARTHR?)

L16 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (L8 OR HEXOSAMINE OR GLUCOSAMINE OR CHONDROITIN(1W)(SULFATE OR SULPHATE OR SO##) OR N(W)(ACETYL OR AC)(1W)(GLUCOSAMINE OR GALACTOSAMINE OR GAL) OR ACETYLGLUCOSAMINE OR ACETYLGALACTOSAMINE OR HEXOSE)

L17 24 L16 NOT L12

L17 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:824333 HCAPLUS

DOCUMENT NUMBER: 139:332195

TITLE: Intra-articular **therapy** in **osteoarthritis**

AUTHOR(S): Uthman, I.; Raynauld, J.-P.; Haraoui, B.
CORPORATE SOURCE: Department of Internal Medicine, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
SOURCE: Postgraduate Medical Journal (2003), 79(934), 449-453
CODEN: PGMJAO; ISSN: 0032-5473
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The medical literature was reviewed from 1968-2002 using Medline and the key words "intra-articular" and "**osteoarthritis**" to determine the various intro-articular **therapies** used in the **treatment** of **osteoarthritis**. Corticosteroids and **hyaluronic** acid are the most frequently used intro-articular **therapies** in **osteoarthritis**. Other intra-articular substances such as orgotein, radiation synovectomy, dextrose prolotherapy, silicone, saline lavage, saline injection without lavage, analgesic agents, non-steroidal anti-inflammatory drugs, **glucosamine**, somatostatin, sodium pentosan polysulfate, chloroquine, mucopolysaccharide polysulfuric acid ester, lactic acid solution, and thiotepa cytostatica have been investigated as potentially therapeutic in the treatment of arthritic joints. Despite the lack of strong, convincing, and reproducible evidence that any of the intro-articular **therapies** significantly alters the progression of **osteoarthritis**, corticosteroids and **hyaluronic** acid are widely used in patients who have failed other **therapeutic** modalities for lack of efficacy or toxicity. As a practical approach for a knee with effusion, steroid injections should be considered while the presence of symptomatic "dry" knees may favor the **hyaluronic** acid approach. The virtual absence of serious side effects, coupled with the perceived benefits, make these approaches attractive.

IT **9004-61-9**, **Hyaluronic** acid
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of intra-articular corticosteroids and **hyaluronic** acid in **treatment** of **osteoarthritis**)

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:551532 HCAPLUS
DOCUMENT NUMBER: 139:99863
TITLE: Glycans involved in the transmigration of leukocytes across the endothelium
INVENTOR(S): Freeze, Hudson; Srikrishna, Geetha; Varki, Ajit; Varki, Nissi
PATENT ASSIGNEE(S): The Regents of the University of California, USA; The Burnham Institute
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003057715 | A2 | 20030717 | WO 2002-US41588 | 20021227 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-346405P P 20011228

AB The authors disclose the identification of glycans involved in the inflammatory response. In particular, the present invention provides novel antibodies directed against novel glycans that are enriched on endothelial cell surfaces. The authors also disclose methods and compns. suitable to mediate the inflammatory response in various settings, as well as methods and compns. for the identification of other inflammatory response mediators.

IT **9004-61-9D, Hyaluronic** acid, glycosaminoglycans-containing **9007-28-7D, Chondroitin sulfate**, glycosaminoglycans-containing
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibodies to carboxylated glycans without reactivity for)

L17 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:511513 HCAPLUS
DOCUMENT NUMBER: 139:63367
TITLE: Oligomer-based method of modulating the release of saccharides, and therapeutic uses thereof
INVENTOR(S): Boucher, Isabelle; Brunet, Serge
PATENT ASSIGNEE(S): ISM Biopolymer Inc., Can.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003054208 | A2 | 20030703 | WO 2002-CA1917 | 20021212 |
| WO 2003054208 | A3 | 20031009 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU,

MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-339339P P 20011213

AB The invention provides a method for the controlled release of saccharides and oligosaccharides in humans and animals. Polysaccharides are digested in a manner to provide oligomers having desired nos. of units of saccharides or monosaccharides, most particularly **glucosamine** and N-**acetylglucosamine** and derivs. thereof. The rate of release of monosaccharides is proportional to the length of the oligomers administered to an organism, and has targeted physiol. effects depending on the length of the oligomers used. The methodol. and compns. of the invention are useful for the delayed delivery of chondroprotective, chondrosynthesis-stimulating agents.

IT **1811-31-0**, N-**Acetylgalactosamine** **1811-31-0D**, N-**Acetylgalactosamine**, derivs. **3416-24-8**, **Glucosamine** **3416-24-8D**, **Glucosamine**, derivs. **7512-17-6**, N-**Acetylglucosamine** **7512-17-6D**, N-**Acetylglucosamine**, derivs.
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligomer-based method of modulating saccharide release, and therapeutic use)

IT **9004-61-9**, **Hyaluronan** **9004-61-9D**, **Hyaluronan**, derivs.
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligomer-based method of modulating saccharide release, and therapeutic use)

L17 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:396729 HCAPLUS
DOCUMENT NUMBER: 138:390973
TITLE: Mixture of sodium hyaluronate and **chondroitin sulfate** for the **treatment** of **osteoarthritis**.
INVENTOR(S): Hermida Ochoa, Elias Humberto
PATENT ASSIGNEE(S): Mex.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003041724 | A1 | 20030522 | WO 2002-EP12703 | 20021113 |

W: AE, AG, AL, AU, AZ, BA, MA, MD, MG, MK, MX, NO, NZ, PL, PT, SD, SE, UZ, VN, YU, ZA, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TD, UG, ZM, BG, CH, CY, CZ, DK, EE, ES, FI, FR, GB, GR, IE, LU, MC, PT, SE, TR, BF, CG, CI, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: MX 2001-11542 A 20011113
US 2002-82743 A 20020222

AB The composition formed by Na hyaluronate and Na **chondroitin sulfate** is used for the **treatment** of chondral lesions in **osteoarthritis** and regeneration of articular

cartilage, tested by injection to knee and hip joints.

IT **9004-61-9, Hyaluronic** acid **9007-28-7, Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(injection viscoelastic solution of sodium hyaluronate and **chondroitin sulfate** for **treatment** of **osteoarthritis** in joints)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:355603 HCAPLUS
DOCUMENT NUMBER: 138:348755
TITLE: **Chondroitin sulfate** containing viscoelastics for use in treating joints
INVENTOR(S): Jafari, Masoud R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 857,543.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003086899 | A1 | 20030508 | US 2002-293094 | 20021113 |
| WO 2001068079 | A2 | 20010920 | WO 2001-US8064 | 20010314 |
| WO 2001068079 | A3 | 20020725 | | |
| W: AU, BR, CA, CN, JP, MX, PL, US, ZA | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| US 2002169142 | A1 | 20021114 | US 2001-857543 | 20010606 |
| US 6632423 | B2 | 20031014 | | |

PRIORITY APPLN. INFO.:
US 2000-189179P P 20000314
WO 2001-US8064 W 20010314
US 2001-857543 A2 20010606

AB Disclosed are viscoelastic compns. and methods of their use in **treating** joints, especially in conjunction with trauma and **osteoarthritis**. An otic viscoelastic formulation containing 1.6 % HMW **hyaluronic** acid and 4 % **chondroitin sulfate** in Viscoat Buffer was found to be superior in terms of retention and duration in the middle ear of Mongolian gerbils.

IT **9004-61-9, Hyaluronic** acid **9007-28-7, Chondroitin sulfate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**chondroitin sulfate**-containing viscoelastics for use in treating joints)

L17 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:202468 HCAPLUS
DOCUMENT NUMBER: 138:215357
TITLE: Use of annellated pyrrole compounds in the treatment of articular cartilage or subchondral

bone degeneration

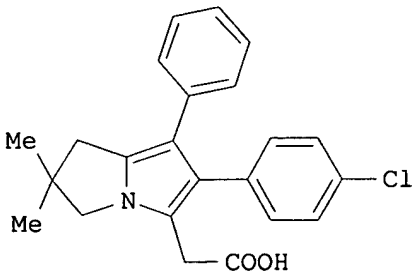
INVENTOR(S): Pelletier, Jean-Pierre; Martel-Pelletier, Johanne
PATENT ASSIGNEE(S): Merckle G.m.b.H., Germany; Ascentia Pharma Inc.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003020267 | A1 | 20030313 | WO 2002-EP9658 | 20020829 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CA 2001-2356099 A 20010830
US 2001-315773P P 20010830

OTHER SOURCE(S): MARPAT 138:215357
GI



I

AB Treating or preventing degeneration or destruction of articular cartilage and/or subchondral bone in the affected joint of a mammal is accomplished by administering an annellated pyrrole compound (Markush included). A preferred compound is I (ML3000). The treatment ameliorates, diminishes, actively treats, reverses, or prevents any injury, damage, or loss of articular cartilage or subchondral bone subsequent to the early stage of the degeneration.

IT **3416-24-8, Glucosamine 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin sulfate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(annellated pyrrole compds. for treatment of articular cartilage or subchondral bone degeneration, and use with other agents)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154262 HCAPLUS
DOCUMENT NUMBER: 138:198610
TITLE: Compositions for the treatment and prevention of pain and inflammation with a cyclooxygenase-2 selective inhibitor and **chondroitin sulfate**
INVENTOR(S): Pulaski, Steven P.; Kundel, Susan
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003015799 | A1 | 20030227 | WO 2002-US25673 | 20020813 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003114416 | A1 | 20030619 | US 2002-215539 | 20020809 |

PRIORITY APPLN. INFO.: US 2001-312211P P 20010814
US 2002-215539 A 20020809

OTHER SOURCE(S): MARPAT 138:198610

AB A method of treating, preventing, or inhibiting pain, inflammation, or inflammation-associated disorder in a subject in need of such treatment or prevention includes treating the subject with **chondroitin sulfate** and a cyclooxygenase-2 selective inhibitor, or a prodrug thereof, wherein the amount of **chondroitin sulfate** and the amount of a cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof together constitute a pain- or inflammation-suppressing treatment or prevention effective amount **Glucosamine** can optionally be present. Compns. that contain the combination of **chondroitin sulfate** and cyclooxygenase-2 selective inhibitor and, optionally, the **glucosamine**, are disclosed, as are pharmaceutical compns.

IT **7512-17-6, N-Acetyl-D-glucosamine 9004-61-9D, Hyaluronic** acid, **glucosamine**-containing **9007-28-7, Chondroitin sulfate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor and **chondroitin**

**sulfate** for treatment and prevention of pain and inflammation)

IT **3416-24-8, Glucosamine 3416-24-8D, Glucosamine**, acid salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor and **chondroitin sulfate** for treatment and prevention of pain and inflammation, and use with **glucosamine**)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:23523 HCAPLUS
DOCUMENT NUMBER: 138:66681
TITLE: Thiazolium as cross-link reversing agents for collagenous proteins
INVENTOR(S): Sander, Tom; Donda, Russell S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003008817 | A1 | 20030109 | US 2001-898913 | 20010703 |
| PRIORITY APPLN. INFO.: | | | US 2001-898913 | 20010703 |

AB The present invention generally relates to compns. and methods for restoring normal mech. properties to collagenous tissue damaged as a result of the natural aging process in mammals. Accordingly, compns. are disclosed which comprises one or more thiazolium based agents capable of inhibiting and reversing non-enzymic crosslinking of collagenous proteins, combined with one or more viscosupplement agents useful in replenishing structural and support material of a tissue or joint, which have been destroyed or damaged over time. The method comprises contacting the target tissue or joint capsule with the composition Administration of the disclosed compds. can stop the progression of, or completely cure degenerative joint diseases. For example, a combined **treatment** with 1 mg/kg of thiazolium salt and 16 mg of Synvisc was effective in **treating** damaged tissue and restoring normal function to a knee joint in patients with knee **osteoarthritis**.

IT **9004-61-9, Hyaluronic** acid **9007-28-7, Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; thiazolium in treatment of joint degeneration by inhibiting and revering crosslinking of collagenous proteins)

L17 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:9699 HCAPLUS
DOCUMENT NUMBER: 139:143552
TITLE: Effects of intra-articular injection of **hyaluronan** on papain-induced hydrarthrosis of knee in rabbits

AUTHOR(S): Matsuzaka, Satoshi; Miyauchi, Satoshi; Horie, Katsuyuki
CORPORATE SOURCE: Medical Research Pharmacology, Tokyo Research Institute, Seikagaku Corporation, Higashi-yamatoshi, Tokyo, Japan
SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 363-368. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK. CODEN: 69DKVZ; ISBN: 1-85573-570-9
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Intra-articular injection of sodium **hyaluronan** (Na-**HA**) is widely applied in the **treatment** of **osteoarthritis**. Na-HA reduces hydrarthrosis accompanied with improvement of synovitis. However, the mol. weight dependence or the mechanism of the effect of Na-HA on the hydrarthrosis is unclear. The objective of the present study is to investigate an effect of various mol. wts. of Na-HA on an exptl. acute hydrarthrosis of knee in rabbits. Highly purified Na-HA prepns. driven from chicken combs, their average mol. weight 30+104 (30Na-HA group), 84+104 (84Na-HA group) and 190+104 (190Na-HA group), were used. The exptl. acute hydrarthrosis was induced by intra-articular injection of papain at 1.5mg/150 μL/joint. On the next day, Na-HA was injected one time intra-articularly at a dose of 1.5mg/150 μL/joint. Animals were sacrificed on the seventh day after the intra-articular injection of Na-HA. Synovial fluid volume (SFV), total protein (TP), **hyaluronan** (**HA**) and **chondroitin** 4-**sulfate** (C4S) in the synovial fluids were determined SFV ($p<0.01$), levels of TP ($p<0.05$) and C4S ($p<0.05$) in the synovial fluids were significantly decreased in the 30Na-HA and 84Na-HA groups. However, no effect was observed for all parameters in the 190Na-HA group. These results suggest that Na-HA directly acts on the inflamed synovium. Addnl., an optimal mol. weight of Na-HA will have effect on the exptl. hydrarthrosis.

IT **24967-93-9, Chondroitin** 4-**sulfate**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (response; effects of intra-articular injection of **hyaluronan** on papain-induced hydrarthrosis of knee in rabbits)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:5721 HCAPLUS
DOCUMENT NUMBER: 138:61345
TITLE: Liposomal encapsulation of glycosaminoglycans for the treatment of arthritic joints
INVENTOR(S): Thompson, Jonathan; Niemiec, Susan
PATENT ASSIGNEE(S): Depuy, UK
SOURCE: PCT Int. Appl., 28 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003000190 | A2 | 20030103 | WO 2002-US19716 | 20020620 |
| WO 2003000190 | A3 | 20030306 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-300750P P 20010625
US 2002-386791P P 20020607

AB Liposome-encapsulated glycosaminoglycans, such as **hyaluronic** acid, **chondroitin sulfate**, keratin sulfate, heparin, and dermatan sulfate, for intra-articular administration and **treatment** of **osteoarthritis** is described. For example, **hyaluronic** acid was incorporated into DPPC liposomes using a film hydration method. He final liposomal concentration was 50 mg/mL DPPC and 10 mg/mL **hyaluronic** acid.

IT **9004-61-9**, **Hyaluronic** acid **9007-28-7**, **Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomal encapsulation of glycosaminoglycans for **treatment** of **osteoarthritis**)

L17 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:4784 HCAPLUS
DOCUMENT NUMBER: 138:61269
TITLE: A complex comprising OCIF and polysaccharide
INVENTOR(S): Yamamoto, Shinichi; Okada, Junichi; Kurihara, Atsushi; Numazawa, Taku; Kondo, Junichi; Tsuda, Eisuke; Mochizuki, Shinichi; Nishi, Hirotaka; Miyazaki, Hideki
PATENT ASSIGNEE(S): Sankyo Company Limited, Japan
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1270015 | A2 | 20030102 | EP 2002-254497 | 20020626 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | | |
|---|---|---|---|---|
| US 2003045456 | A1 | 20030306 | US 2002-183091 | 20020627 |
| ZA 2002005164 | A | 20030324 | ZA 2002-5164 | 20020627 |
| NO 2002003144 | A | 20021230 | NO 2002-3144 | 20020628 |
| JP 2003160601 | A2 | 20030603 | JP 2002-190407 | 20020628 |
| BR 2002002439 | A | 20030610 | BR 2002-2439 | 20020628 |
| SG 98059 | A1 | 20030820 | SG 2002-3944 | 20020628 |

CN 1442201 A 20030917 CN 2002-155849 20020629
US 2003139325 A1 20030724 US 2003-364045 20030211
PRIORITY APPLN. INFO.: JP 2001-198985 A 20010629
US 2002-183091 A1 20020627

AB A novel complex comprising at least one substance selected from the group consisting of osteoclastogenesis-inhibitory factor (OCIF), analogs thereof, and variants thereof, which is bound to at least one substance selected from the group consisting of polysaccharides and derivs. thereof shows prolonged retention in the bloodstream after administration making it useful in the treatment and prophylaxis of bone metabolic diseases.

IT **9004-61-9**, **Hyaluronic** acid **9007-28-7**, **Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complex comprising OCIF and polysaccharide for treatment of bone metabolic diseases)

L17 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:876095 HCAPLUS
DOCUMENT NUMBER: 139:73863
TITLE: Various interactions of drugs with cross-linked hyaluronate gel
AUTHOR(S): Yomota, Chikako; Okada, Satoshi
CORPORATE SOURCE: National Institute of Health Sciences Osaka, Osaka, 540-0006, Japan
SOURCE: ACS Symposium Series (2003), 833(Polymer Gels), 326-338
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Hyaluronate**(**HA**) is a biopolymer composed of repeating disaccharide subunits of **N-acetyl**-D-**glucosamine** and D-glucuronate. HA is extensively distributed in connective tissue, synovial fluid of joints and in vitreous humor of the eye. It has been extensively used as a **therapeutic** agent in **osteoarthritis** and ophthalmic surgery. Thus hyaluronate is one of the natural polymers successfully applicable to the biomedical use. The basic properties of crosslinked HA gel have been reported(1) and there are several reports of applying the HA gel to medical devices(2,3). However it is reported that due to the high swelling, the ability of the HA gel to retain other substances is not strong enough to use as a pharmaceutical reservoir(2). Previously we noted the reports that some anionic polymer gels bind cationic surfactants(4,5). We have already reported that dodecyltrimethylammonium bromide(DOTMA) binds HA in solution cooperatively and that the binding constant is much smaller than those of other anionic polysaccharides such as **chondroitin sulfate**(6). Furthermore the crosslinked HA gel was observed to shrink with time in addition of DOTMA, and the weight of the gel decreased by only 2-4% of the initial weight(7). On the other hand, it is well known that many kinds of drugs have properties of surfactants, and self association (micelle) in aqueous solution have been investigated(8-13). Therefore as cationic surfactants, some drugs were expected to cause the shrinking of the HA gel. The interactions of the crosslinked HA gel with several kinds of cationic drugs were investigated, and the release of incorporated

substances was measured.
IT **9004-61-9, Hyaluronic** acid
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interactions of drugs with cross-linked hyaluronate gel)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:737518 HCAPLUS
DOCUMENT NUMBER: 138:378314
TITLE: Oral and intra-articular remedies: Review of papers published from March 2001 to February 2002
AUTHOR(S): Jubb, Ronald W.
CORPORATE SOURCE: Selly Oak Hosp., Univ. Birmingham, Birmingham, UK
SOURCE: Current Opinion in Rheumatology (2002), 14(5), 597-602
CODEN: CORHES; ISSN: 1040-8711
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. There have been considerable advances in the drug **treatments** used to **treat osteoarthritis**. The development of selective cyclooxygenase inhibitors (COX-II) and confirmation of their efficacy and gastrointestinal safety will reduce treatment morbidity in the elderly. Guidelines for safe and appropriate use of COX-II drugs are now available. The role of antiinflammatory drugs in precipitating cardiorenal events has been highlighted but remains to be fully evaluated. **Glucosamine**, diacerein, and **hyaluronan** may all be disease-modifying drugs for osteoarthritis but confirmatory studies are still needed.
IT **3416-24-8, Glucosamine 9004-61-9, Hyaluronan**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral and intra-articular remedies for **treatment** of **osteoarthritis**)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:429542 HCAPLUS
DOCUMENT NUMBER: 137:11003
TITLE: Chondroprotective/restorative compositions containing **hyaluronic** acid
INVENTOR(S): Pierce, Scott W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002068718 | A1 | 20020606 | US 2001-967977 | 20011002 |

PRIORITY APPLN. INFO.: US 2000-237838P P 20001003

AB An oral composition based on **hyaluronic** acid or its salts and optionally a **therapeutic** drug is provided for **treating** or **preventing osteoarthritis**, joint effusion, joint inflammation and pain, synovitis, lameness, post-operative arthroscopic surgery, deterioration of proper joint function including joint mobility, the reduction or inhibition of metabolic activity of chondrocytes, the activity of enzymes that degrade cartilage, and the reduction or inhibition of the production of **hyaluronic** acid in a mammal. Addnl., compns. containing **hyaluronic** acid, **chondroitin sulfate** and **glucosamine** sulfate in a paste formulation are also described which can be administered on their own or can be used as a feed additive for cats and dogs. For example, a composition contained (by weight) **glucosamine** sulfate 36%, **chondroitin sulfate** 4%, sodium hyaluronate 0.144%, manganese sulfate 0.144%, ibuprofen 200 mg, powdered sugar 20%, glycerin 0.7%, xanthan gum 0.2%, sodium benzoate 0.7%, citric acid 0.2%, molasses 23.5%, and water 14.4%.

IT **9004-61-9**, **Hyaluronic** acid **9007-28-7**, **Chondroitin sulfate**
RL: FFD (Food or feed use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chondroprotective/restorative compns. containing **hyaluronic** acid for treatment of joint disorders)

L17 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:869012 HCAPLUS
DOCUMENT NUMBER: 136:11162
TITLE: Analgesics combined with naturally-occurring chondroprotective agents
INVENTOR(S): Hammerly, Milton
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2001046971 | A1 | 20011129 | US 2001-784384 | 20010215 |
| US 6608041 | B2 | 20030819 | | |

PRIORITY APPLN. INFO.: US 2000-183704P P 20000218

AB Pharmaceutical compns. comprise a chondroprotective component and an analgesic component, wherein the chondroprotective component is naturally occurring in a preferred form of the invention, and the analgesic component is acetaminophen or its derivs. or analogs. The invention also provides procedures for administering the compns. to a patient who is afflicted with osteoarthritis. Acetaminophen 400 and **chondroitin sulfate** 150 g are placed into a mech. mixer and shaken until a homogeneous mixture is obtained. The composition is suitable to be administered to a mammalian subject for the **treatment** of **osteoarthritis** by ingestion of 5.5 g

of such a mixture on a daily basis.

IT **7512-17-6, N-Acetyl glucosamine**
**9004-61-9, Hyaluronan 9007-28-7,**
**Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesics combined with naturally-occurring chondroprotective agents)

L17 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:138996 HCAPLUS
DOCUMENT NUMBER: 134:309144
TITLE: Water-exchange processes in hyaline cartilage and in its major components in normal and osteoarthrosis cartilage
AUTHOR(S): Nikolaeva, S. S.; Chhol, Kim Zong; Bykov, V. A.; Roshina, A. A.; Yakovleva, L. B.; Korolyova, O. A.; Omelianenko, N. P.; Rebrov, L. B.
CORPORATE SOURCE: Sci. Res. Sch., Methodical Center Biomedical Technology, Moscow, 123056, Russia
SOURCE: Voprosy Meditsinskoi Khimii (2000), 46(6), 581-590
CODEN: VMDKAM; ISSN: 0042-8809
PUBLISHER: NII Biomeditsinskoi Khimii
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The content of different forms of tissue water was studied in the normal articular cartilage and osteoarthrosis cartilage and its structural components: collagen, potassium hyaluronate, sodium **chondroitin sulfate** and its complexes. In the components of cartilage matrix a few of fractions of bound water different in the strength of binding are present. At the maximal humidity, all water in collagen binds with the active groups of biopolymers and in the glycosaminoglycans, in addition to bound water, are present, two crystal forms of freezing water (free water) at least. The quantity of free water in the collagen-**chondroitin sulfate** membrane, is increased with the increase of **chondroitin sulfate**. In the collagen-hyaluronate complex, fraction of free water is found only at the low concentration of potassium hyaluronate. It was shown that in the hyalin cartilage, in different from the other connective tissues (skin, Achilles tendon), the most part of water is free water and its quantity is increased in the osteoarthrosis. It is supposed that the rearrangement of binding and free-water fractions in the **osteoarthrosis** is the result of deficiency of **hyaluronic** acid and therefore this may be regarded in the improvement of methods of **treatment**. This scientific and methodical approach allow to receive information on the forms and binding energy of water in the biol. tissues, which is absorbed from fluids and steam phase and determine characters of the pathol. changes.

L17 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:450288 HCAPLUS
DOCUMENT NUMBER: 133:290516
TITLE: Sulfated glycosaminoglycans and **glucosamine** may synergize in promoting synovial **hyaluronic** acid synthesis
AUTHOR(S): McCarty, M. F.; Russell, A. L.; Seed, M. P.
CORPORATE SOURCE: NutriGuard Research, La Jolla, CA, 92037, USA

SOURCE: Medical Hypotheses (2000), 54(5), 798-802
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 48 refs. is given. High-mol.-weight **hyaluronic** acid (**HA**) produced by the synovium may function physiol. to aid preservation of cartilage structure and **prevent** arthritic pain; both the size and concentration of HA in synovial fluid are diminished in **osteoarthritis** (OA). **Glucosamine** therapy for OA can be expected to increase synovial HA production by providing rate-limiting substrate. In addition, certain sulfated glycosaminoglycans and polysaccharides - including **chondroitin sulfate** (CS), dermatan sulfate, and pentosan polysulfate - stimulate synovial HA production, apparently owing to a hormone-like effect triggered by the binding of these polymers to membrane proteins of synovial cells. Surprisingly, a proportion of orally administered CS is absorbed as intact polymers - apparently by pinocytosis. These considerations may rationalize clin. studies concluding that oral CS provides slow-onset but durable pain relief and functional improvement in OA. The possibility that oral **glucosamine** and CS may interact in a complementary or synergistic fashion to improve synovial fluid HA content in OA should be assessed in clin. studies, and the potential of adjunctive CS administration to improve the clin. response achievable with optimal intakes of **glucosamine** should likewise be evaluated. In light of the fact that the synovium virtually functions as a 'placenta' for cartilage, focusing on synovium as the target for therapeutic intervention in OA may be a rational strategy.

IT **3416-24-8, Glucosamine 9007-28-7, Chondroitin sulfate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfated glycosaminoglycans and **glucosamine** synergize in promoting synovial **hyaluronic** acid synthesis)

IT **9004-61-9, Hyaluronic** acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sulfated glycosaminoglycans and **glucosamine** synergize in promoting synovial **hyaluronic** acid synthesis)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:807322 HCAPLUS
DOCUMENT NUMBER: 132:245687
TITLE: Niacinamide **therapy** for **osteoarthritis** - does it inhibit nitric oxide synthase induction by interleukin-1 in chondrocytes?
AUTHOR(S): McCarty, M. F.; Russell, A. L.
CORPORATE SOURCE: Nutrition 21/AMBI, San Diego, CA, 92037, USA
SOURCE: Medical Hypotheses (1999), 53(4), 350-360
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 157 refs. Fifty years ago, Kaufman reported that high-dose niacinamide was beneficial in osteoarthritis (OA) and rheumatoid arthritis. A recent double-blind study confirmed the efficacy of niacinamide in OA. It may be feasible to interpret this finding in the context of evidence that synovium-generated interleukin-1 (IL-1), by inducing NO synthase and thereby inhibiting chondrocyte synthesis of aggrecan and type II collagen, is crucial to the pathogenesis of OA. Niacinamide and other inhibitors of ADP ribosylation have been shown to suppress cytokine-mediated induction of NO synthase in a number of types of cells; it is therefore reasonable to speculate that niacinamide will have a comparable effect in IL-1-exposed chondrocytes, blunting the antianabolic impact of IL-1. The chondroprotective antibiotic doxycycline may have a similar mechanism of action. Other nutrients reported to be useful in OA may likewise intervene in the activity or synthesis of IL-1. Supplemental **glucosamine** can be expected to stimulate synovial synthesis of **hyaluronic** acid; **hyaluronic** acid suppresses the anticatabolic effect of IL-1 in chondrocyte cell cultures, and has documented therapeutic efficacy when injected intra-articularly. S-adenosylmethionine (SAM), another proven therapy for OA, upregulates the proteoglycan synthesis of chondrocytes, perhaps because it functions physiol. as a signal of sulfur availability. IL-1 is likely to decrease SAM levels in chondrocytes; supplemental SAM may compensate for this deficit. Adequate Se nutrition may down-regulate cytokine signaling, and ample intakes of fish oil can be expected to decrease synovial IL-1 production; these nutrients should receive further evaluation in OA. These considerations suggest that nontoxic nutritional regimens, by intervening at multiple points in the signal transduction pathways that promote the synthesis and mediate the activity of IL-1, may provide a substantially superior alternative to nonsteroidal anti-inflammatory drugs (merely palliative and often dangerously toxic) in the treatment and perhaps prevention of OA.
REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:9887 HCAPLUS
DOCUMENT NUMBER: 130:71612
TITLE: Bioresorbable antiadhesion of carboxypolysaccharide polyether intermacromolecular complexes and methods for their use in reducing surgical adhesions
INVENTOR(S): Schwartz, Herbert E.; Blackmore, John M.
PATENT ASSIGNEE(S): Fziomed, Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

WO 9858011 A1 19981223 WO 1998-US10814 19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
US 5906997 A 19990525 US 1997-877649 19970617
US 6017301 A 20000125 US 1998-23267 19980213
US 6034140 A 20000307 US 1998-23097 19980213
AU 9876985 A1 19990104 AU 1998-76985 19980528
AU 754787 B2 20021128
EP 1002002 A1 20000524 EP 1998-924928 19980528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002511897 T2 20020416 JP 1999-504437 19980528
US 6133325 A 20001017 US 1999-252147 19990218
PRIORITY APPLN. INFO.: US 1997-877649 A 19970617
WO 1998-US10814 W 19980528

AB The present invention relates to improved methods for making and using bioadhesive, bioresorbable, antiadhesion compns. made of intermacromol. complexes of carboxyl-containing polysaccharides and polyethers, and to the resulting compns. The polymers are associated with each other, and are then either dried or are used as fluids. Bioresorbable, bioadhesive, antiadhesion compns. are useful in surgery to prevent the formation of post-surgical adhesions. The compns. are designed to breakdown in vivo, and thus be removed from the body. Membranes are inserted during surgery either dry or optionally after conditioning in aqueous solns. The antiadhesion, bioadhesive, bioresorptive, antithrombogenic and phys. properties of such membranes can be varied as needed by carefully adjusting the pH of the polymer casting solns., polysaccharide composition, the polyether composition, or by conditioning the membranes prior to surgical use. Bi- or multi-layered membranes can be made and used to provide further control over the phys. and biol. properties of antiadhesion membranes. Antiadhesion compns. may also be used to deliver drugs to the surgical site and release them locally.

IT **9004-61-9**, **Hyaluronic** acid **9007-28-7**, **Chondroitin sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioresorbable adhesives containing carboxypolysaccharide-polyether intermacromol. complexes)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:699598 HCAPLUS
DOCUMENT NUMBER: 130:93516
TITLE: Roles of aggrecan, a large **chondroitin sulfate** proteoglycan, in cartilage structure and function
AUTHOR(S): Watanabe, Hideto; Yamada, Yoshihiko; Kimata, Koji
CORPORATE SOURCE: Craniofacial Developmental Biology and Regeneration Branch, National Institute of

Dental Research, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Biochemistry (Tokyo) (1998), 124(4), 687-693
CODEN: JOBIAO; ISSN: 0021-924X
PUBLISHER: Japanese Biochemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 62 refs. on structure and function of aggrecan and its genetic disorders. Aggrecan, a large aggregating proteoglycan, is one of the major structural components of cartilage. Its core protein contains three globular domains and two glycosaminoglycan-attachment domains. These domains play various roles to maintain cartilage structure and function. An N-terminal globular domain binds **hyaluronan** and link protein to form huge aggregates. The **chondroitin sulfate** (CS) chains attach to the CS domain and provide a hydrated, viscous gel that absorbs compressive load. Two autosomal recessive chondrodysplasias, cartilage matrix deficiency (cmd) in mice and nanomelia in chicken are both caused by aggrecan gene mutations. Cmd homozygotes die shortly after birth, while the heterozygotes are born normal. However, cmd heterozygotes develop late onset of spinal disorder, which suggests aggrecan as a candidate gene predisposing individuals to spinal problems. Nanomelia is a useful model to elucidate intracellular trafficking of proteoglycans. Further studies on aggrecan will lead to prophylaxis and **treatment** of joint destructive diseases such as **osteoarthrosis** and to elucidation of cartilage development, which is essential for skeletal formation.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:862804 HCAPLUS
DOCUMENT NUMBER: 123:305923
TITLE: Biochemical and pharmacokinetic aspects of oral treatment with **chondroitin sulfate**
AUTHOR(S): Conte, A.; Volpi, N.; Palmieri, L.; Bahous, I.; Ronca, G.
CORPORATE SOURCE: Dep. "Biologia Animale", Univ. Modena, Italy
SOURCE: Arzneimittel-Forschung (1995), 45(8), 918-25
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Chondroitin sulfate** (Condrosulf) was characterized for structure, physicochem. properties and purity. This glycosaminoglycan has a relative mol. mass of about 14,000 a sulfate-to-carboxyl ratio of 0,95 due to the high percentage of monosulfated disaccharides (38% 6-monosulfate and 55% 4-monosulfate) and a low amount of disulfated disaccharides (1.1%) inside the polysaccharide chains. No other glycosaminoglycans were detected in the preparation **Chondroitin sulfate** was labeled by reduction with sodium 3H-borohydride and administered by oral route in the rat and dog. More than 80% of radioactivity was absorbed and found in urine and tissues. The plasma radioactivity was

fractionated by size-exclusion chromatog. in three fractions: radioactivity associated with high, intermediate and low mol. mass compds. The peak value of the concentration of high mol. mass radioactivity compds. in plasma was reached after 1.6 and 2.1 h for the rat and dog, resp. After 36 h the high mol. mass radioactivity compds. were still present in plasma of dog and rat. After 24 h radioactivity was higher in the intestine, liver, kidneys, synovial fluid and cartilage than in other tissues. **Chondroitin sulfate** was orally administered to man (healthy volunteer) in a single daily dose of 0.8 g and in two daily doses of 0.4 g. The results showed that both forms of administration determined a significant increase of plasma concentration of **chondroitin sulfate** as compared with predose value over a full 24 h period. Elimination constant values and tmax (of the first administration in the case of fractionated dose) were almost the same for the two administrations. Some biochem. parameters (number of leukocytes, proteins, sulfated glycosaminoglycans and **hyaluronic** acid amts., and N-acetylglucosaminidase activity) of synovial fluid were evaluated in controls and **treated osteoarthritic** subjects. No variations were observed in the patient who did not receive **chondroitin sulfate**. Five days of **chondroitin sulfate** administration led to a significant increase of concentration and mol. mass of **hyaluronan** and a decrease of a lysosomal enzyme, N-acetyl-glucosaminidase. No significant differences in leukocyte count and protein content were detected.

IT **9007-28-7, Chondroitin sulfate**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(biochem. and pharmacokinetic aspects of oral treatment with **chondroitin sulfate**)

L17 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:364299 HCAPLUS
DOCUMENT NUMBER: 122:115054
TITLE: Purified natural and synthetic compounds for the **treatment** of **osteoarthritis**
INVENTOR(S): Lansbury, Peter T., Jr.; Hauschka, Peter V.
PATENT ASSIGNEE(S): Neogenix, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9428889 | A1 | 19941222 | WO 1994-US6490 | 19940608 |
| W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, UA, UZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9472058 | A1 | 19950103 | AU 1994-72058 | 19940608 |
| PRIORITY APPLN. INFO.: | | | US 1993-73189 | 19930608 |
| | | | WO 1994-US6490 | 19940608 |

AB The present invention relates to individual, well-defined compds. and the uses of these compds., alone or in conjunction with bioactive mols. such as growth factors or metalloproteinase inhibitors, for the repair of cartilage damage as, for example, is found in osteoarthritis. Such well-defined compds. may include purified components of the extracellular matrix, derivs. of extracellular matrix components, and glycosaminoglycan mimics. The glycosaminoglycan mimics include **chondroitin-4-sulfate**, **chondroitin-6-sulfate**, **hyaluronic** acid, heparin, heparan sulfate, keratan sulfate, dermatan sulfate, poly-N-**acetylglucosamine**, and poly-N-**glucosamine**.

IT **9004-61-9**, **Hyaluronic** acid **24967-93-9**, **Chondroitin-4-sulfate 25322-46-7**, **Chondroitin-6-sulfate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(extracellular matrix components for **treatment** of **osteoarthritis**)

L17 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:48935 HCAPLUS
DOCUMENT NUMBER: 120:48935
TITLE: Novel compositions and methods for detection and **treatment** of human **osteoarthritis**
INVENTOR(S): Sandy, John D.; Flannery, Carl R.; Neame, Peter J.; Lohmander, L. Stefan
PATENT ASSIGNEE(S): Shriners Hospitals for Crippled Children, USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9322429 | A1 | 19931111 | WO 1993-US4029 | 19930429 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5427954 | A | 19950627 | US 1992-875515 | 19920429 |

PRIORITY APPLN. INFO.: US 1992-875515 19920429

AB The monitoring of human aggrecanase activity is used in the detection, **treatment**, and **prevention** of human **osteoarthritis**. The cleavage site where aggrecanase cleaves aggrecan has been identified as the bond between Glu-373 and Ala-374 and this allows the design of inhibitors of the aggrecanase (no data). Synovial fluid from osteoarthritis patients was fractionated in CsCl d. gradients and the **chondroitin sulfate**-rich fraction and a fraction not binding **hyaluronan** and link protein, and therefore lacking the G1 domain was obtained. N-terminal anal. of the cleavage products identified the site of cleavage.

L17 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:605876 HCAPLUS
DOCUMENT NUMBER: 103:205876

TITLE: Effects of sodium diclofenac on glycosaminoglycan metabolism in experimental osteoarthritis in rabbits
AUTHOR(S): Eronen, Ilkka; Videman, Tapio
CORPORATE SOURCE: Inst. Occup. Health, Univ. Cent. Hosp., Helsinki, SF-00170, Finland
SOURCE: Scandinavian Journal of Rheumatology (1985), 14(1), 37-42
CODEN: SJRHAT; ISSN: 0300-9742
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of diclofenac (DS) [15307-86-5] on the metabolism of glycosaminoglycans (GAGs) was studied in rabbits during the development of osteoarthritis of the knee induced by immobilization. DS did not inhibit in vivo metabolism of sulfated GAGs. Healthy rabbits given DS showed only marginal changes of GAG content in joint tissues. DS did not prevent the loss of GAGs from the weight-bearing cartilages of the immobilized knees, but caused a further loss of **chondroitin sulfates** accompanied by an increased amount of **hyaluronic** acid [**9004-61-9**] in the tissues. DS **prevented** the accumulation of GAGs, which normally occurs during development of **osteoarthritis** in tissues of the tibial margin and in collateral ligaments. Thus, the effect of DS on the GAG metabolism in connective tissues is somewhat different from that with other nonsteroidal antiinflammatory agents.

IT **3416-24-8 9007-28-7**
RL: BIOL (Biological study)
(of joint tissues, diclofenac effect on, in osteoarthritis)

IT **9004-61-9**
RL: PROC (Process)
(of joint tissues, diclofenac increase of, in osteoarthritis)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 08:54:48 ON 13 FEB 2004)

| | | |
|---|---|---|
| L1 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON "HYALURONIC ACID"/CN |
| L2 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON HEXOSAMINES/CN |
| L3 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON GLUCOSAMINE/CN |
| L4 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON N-ACETYL-D-GLUCOSAMINE/CN |
| L5 | 1 | SEA FILE=REGISTRY ABB=ON PLU=ON N-ACETYL-D-GALACTOSAMINE/CN |
| L6 | 2 | SEA FILE=REGISTRY ABB=ON PLU=ON HEXOSE/CN |
| L7 | 3 | SEA FILE=REGISTRY ABB=ON PLU=ON "CHONDROITIN SULFATE"/CN OR "CHONDROITIN SULFATE A"/CN OR "CHONDROITIN SULFATE C"/CN |
| L8 | 9 | SEA FILE=REGISTRY ABB=ON PLU=ON L2 OR L3 OR L4 OR L5 OR L6 OR L7 |
| L9 | 15273 | SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HYALURONAN OR HA(3A)HYALURON? |
| L18 | 659 | SEA L9(L)((OSTEOARTHRIT? OR (OSTEO OR DEGENERAT?)(3A)(ARTHRIT? OR ARTHROSIS) OR OSTEOARTHROSIS OR DEGENERAT?(3A)(JOINT(W)(DISEAS? OR DISORDER)))(S)(TREAT? OR THERAP? OR PREVENT?) OR ANTIOSTEOARTHR?) |
| L19 | 75 | SEA L18(L)(L8 OR HEXOSAMINE OR GLUCOSAMINE OR CHONDROITIN (1W)(SULFATE OR SULPHATE OR SO##) OR N(W)(ACETYL OR AC)(1W)(GLUCOSAMINE OR GALACTOSAMINE OR GAL) OR ACETYLGLUCOSAMINE OR ACETYLGALACTOSAMINE OR HEXOSE) |

L20 72 L19 NOT L13

PROCESSING COMPLETED FOR L20
L21 40 DUP REM L20 (32 DUPLICATES REMOVED)

L21 ANSWER 1 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-671402 [63] WPIDS
DOC. NO. CPI: C2003-183116
TITLE: Sterile, aqueous viscoelastic composition useful in ophthalmic surgical procedures comprises a combination of hyaluronic acid and chondroitin sulfate or its salt in a vehicle.
DERWENT CLASS: A96 B04 D22
INVENTOR(S): JAFARI, M R
PATENT ASSIGNEE(S): (ALCO-N) ALCON INC
COUNTRY COUNT: 38
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003057187 | A1 | 20030717 | (200363)* | EN | 21 |

RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
W: AU BR CA CN GB JP KP KR MX NZ PH PL RU SG US ZA

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003057187 | A1 | WO 2002-US36548 | 20021113 |

PRIORITY APPLN. INFO: US 2001-342918P 20011221
AN 2003-671402 [63] WPIDS
AB WO2003057187 A UPAB: 20031001
NOVELTY - A sterile aqueous viscoelastic composition comprises a combination (w/v.%) of **hyaluronic** acid (1 - 2) or its salt and **chondroitin sulfate** (3 - 5, preferably 4) or its salt in a vehicle. The molecular weight of **hyaluronic** acid and **chondroitin sulfate** is 1500000 - 1900000 daltons and 20000 - 100000 (preferably 50000 - 90000) daltons respectively.

ACTIVITY - Ophthalmological; Osteopathic; Antiarthritic; Dermatological.

MECHANISM OF ACTION - None given.

USE - In ophthalmic surgical procedures e.g. cataract surgery (claimed). Also useful for the **treatment** of chondromalacia and **osteoarthritis** (e.g. grade I and grade II **osteoarthritis**); in drug delivery (e.g. delivery of anti-fibrotics, antibiotics, steroidal and non-steroidal antiinflammatories, anesthetics, analgesics, and other medicaments or gene **therapies** to diseased or traumatized tissues), cosmetic surgery and reconstructive surgery; for reducing wrinkles or **treating** varicose veins; and in post-surgical, arising from tissue fibrosis and adhesions (e.g. in nasal, spinal cord, cardiovascular, orthopedic and orthodontic surgical procedures).

ADVANTAGE - The composition exhibits an improved rheological

profile for certain types of surgery, particularly ophthalmic surgery. The composition permits superior performance in ophthalmic surgery, and in particular in the conventional steps or phases in the surgical removal of cataracts. During the surgical procedure, the composition achieves satisfactory intraoccular space maintenance and ocular tissue protection and the same time permits manipulation of ocular tissues and ease of removal at the end of the procedure. The composition provides a physician with functional benefits without the attendant cost and inconvenience of using multiple products/syringes during a single surgical procedure.
Dwg.0/2

L21 ANSWER 2 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-468583 [44] WPIDS
DOC. NO. CPI: C2003-125104
TITLE: Use of a mixture of chondroitin sulfate and hyaluronic acid in the manufacture of medicament for repairing or regenerating cartilage in joints caused by cartilage disease or trauma.
DERWENT CLASS: B05
INVENTOR(S): HERMIDA, O E H
PATENT ASSIGNEE(S): (ALCO-N) ALCON INC
COUNTRY COUNT: 102
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003041724 | A1 | 20030522 | (200344)* | EN | 22 |

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003041724 | A1 | WO 2002-EP12703 | 20021113 |

PRIORITY APPLN. INFO: US 2002-82743 20020222; MX 2001-11542 20011113
AN 2003-468583 [44] WPIDS
AB WO2003041724 A UPAB: 20030710
NOVELTY - Repair or regeneration of a cartilage caused by cartilage disease or trauma involves intraarticular instillation of a mixture of **chondroitin sulfate** (a) and **hyaluronic** acid (b) or its salts.
DETAILED DESCRIPTION - AN INDEPENDENT CLAIM is included for treating joints exhibiting degeneration of articular cartilage involving intraarticular administration of a viscous composition comprising a mixture of (a) and (b) or its salts.
ACTIVITY - Osteopathic; Antiarthritic.
MECHANISM OF ACTION - None given.
USE - The composition is used for repairing or regenerating

cartilage in joints caused by cartilage disease or trauma; and for **treating** joints of knees, shoulders, sacroiliac, coxofemoral, ankles, elbows, interphalangeal and wrists exhibiting; for the **treatment** of degeneration of articular cartilage caused by chondromalacia or **osteoarthritis** of grade I or II in mammals (preferably humans) (claimed).

ADVANTAGE - The composition is stable, sterile, non-pyrogenic, and a viscoelastic solution. The composition has a viscosity of 20000 - 60000 cps and an osmolarity of 300 - 350 mOsmol/kg. The **treatment** regenerates the articular cartilage destroyed by grade I and II **osteoarthritis** by up to 94.5% according to the results obtained from a study made on 325 knees and 16 coxofemoral joints.

Dwg.0/6

L21 ANSWER 3 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-201368 [19] WPIDS
DOC. NO. CPI: C2003-051203
TITLE: Composition, useful for the treatment of arthritic joints, e.g. osteoarthritis, comprises at least one glycosaminoglycan, part of which are encapsulated in liposome.
DERWENT CLASS: B04
INVENTOR(S): NIEMIEC, S; THOMPSON, J
PATENT ASSIGNEE(S): (DEPU-N) DEPUY
COUNTRY COUNT: 100
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003000190 | A2 | 20030103 | (200319)* | EN | 28 |

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003000190 | A2 | WO 2002-US19716 | 20020620 |

PRIORITY APPLN. INFO: US 2002-386791P 20020607; US 2001-300750P 20010625

AN 2003-201368 [19] WPIDS

AB WO2003000190 A UPAB: 20030320

NOVELTY - A composition (C) useful for the treatment of arthritic joints, comprises at least one glycosaminoglycan, at least part of which are encapsulated in at least one liposome.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) Liposomal delivery vehicle (I) which encapsulates one or more glycosaminoglycans; and

(2) Method for the treatment of arthritic joints, comprising:

(a) preparing (C); and
(b) administering (C).
ACTIVITY - Antiarthritic; Osteopathic.
No biological data available.
MECHANISM OF ACTION - None given.
USE - (C) is useful for the treatment of arthritic joints, e.g. osteoarthritis (claimed), by preparing (C) and administering (C) in an appropriate dosage.
Dwg.0/0

L21 ANSWER 4 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-081566 [08] WPIDS
CROSS REFERENCE: 1996-309308 [31]; 1997-341293 [31]; 1998-494554 [42]; 1998-567506 [48]; 1999-119663 [10]; 1999-130297 [11]; 2000-339499 [29]; 2000-339500 [29]; 2000-349544 [30]; 2000-350329 [30]; 2000-350330 [30]; 2000-365358 [31]; 2001-182720 [18]; 2001-380485 [40]; 2001-388427 [41]; 2001-556526 [62]; 2002-017246 [02]; 2002-074189 [10]; 2002-616543 [66]; 2003-379050 [36]; 2003-645129 [61]; 2003-721614 [68]; 2003-851612 [79]; 2004-021100 [02]
DOC. NO. CPI: C2004-033462
TITLE: New targeted drug delivery system comprising chondroprotective agents, useful for inhibiting cartilage degradation, specifically for reducing or preventing destruction of articular cartilage in a joint.
DERWENT CLASS: A96 B04 B07 D16
INVENTOR(S): DEMOPULOS, G A; HERZ, J M; PALMER, P P
PATENT ASSIGNEE(S): (OMER-N) OMEROS CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2003235589 | A1 | 20031225 | (200408)* | | 71 |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| US 2003235589 | A1 | Provisional | US 1998-105026P | 19981020 |
| | | Provisional | US 1998-107256P | 19981105 |
| | | Provisional | US 1999-144904P | 19990721 |
| | | CIP of | WO 1999-US24625 | 19991020 |
| | | CIP of | WO 1999-US26330 | 19991105 |
| | | CIP of | WO 2000-US19864 | 20000721 |
| | | CIP of | US 2001-839633 | 20010420 |
| | | CIP of | US 2002-31546 | 20020118 |
| | | Provisional | US 2002-353552P | 20020201 |
| | | | US 2003-356649 | 20030131 |

PRIORITY APPLN. INFO: US 2003-356649 20030131; US 1998-105026P 19981020; US 1998-107256P 19981105; US 1999-144904P 19990721; WO 1999-US24625 19991020; WO 1999-US26330 19991105; WO

2000-US19864 20000721; US 2001-839633 20010420; US 2002-31546 20020118; US 2002-353552P 20020201

AN 2004-081566 [08] WPIDS

CR 1996-309308 [31]; 1997-341293 [31]; 1998-494554 [42]; 1998-567506 [48]; 1999-119663 [10]; 1999-130297 [11]; 2000-339499 [29]; 2000-339500 [29]; 2000-349544 [30]; 2000-350329 [30]; 2000-350330 [30]; 2000-365358 [31]; 2001-182720 [18]; 2001-380485 [40]; 2001-388427 [41]; 2001-556526 [62]; 2002-017246 [02]; 2002-074189 [10]; 2002-616543 [66]; 2003-379050 [36]; 2003-645129 [61]; 2003-721614 [68]; 2003-851612 [79]; 2004-021100 [02]

AB US2003235589 A UPAB: 20040202

NOVELTY - A targeted drug delivery system for the protection of cartilage, comprising chondroprotective agents contained within a delivery vehicle coupled to an antibody or antibody fragment specific to an antigenic determinant localized within the joint, is new. The chondroprotective agents include at least one anabolic chondroprotective agent and at least one inhibitor of cartilage catabolism to inhibit cartilage catabolism and promote cartilage anabolism.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a targeted composition for the protection of cartilage comprising several chondroprotective agents in a carrier, at least one chondroprotective agent is coupled to an antibody or antibody fragment specific to an antigenic determinant localized within the joint, where the chondroprotective agents include at least one anabolic chondroprotective agent and at least one inhibitor of cartilage catabolism, each being included to inhibit cartilage catabolism and promote cartilage anabolism; and

(2) protecting cartilage in a patient by delivering a targeted drug delivery system defined above.

ACTIVITY - Osteopathic; Antiarthritic; Antirheumatic; Antiinflammatory; Dermatological; Immunosuppressive.

Experimental protocols are described but no results are given.

MECHANISM OF ACTION - Gene Therapy.

USE - The targeted delivery system is useful for inhibiting cartilage degradation, specifically for reducing or preventing destruction of articular cartilage in a joint. It may also be used for treating polyarticular osteoarthritis, (juvenile) rheumatoid arthritis, neuropathic arthropathy, acute rheumatic fever, ochronosis, systemic lupus erythematosus, psoriatic arthritis; ankylosing spondylitis, and other spondyloarthropathies and crystalline arthropathies.

Dwg.0/9

L21 ANSWER 5 OF 40 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003612008 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 14651444

TITLE: Glucosamine: a review of its use in the management of osteoarthritis.

AUTHOR: Matheson Anna J; Perry Caroline M

CORPORATE SOURCE: Adis International Limited, Auckland, New Zealand.

SOURCE: Drugs & aging, (2003) 20 (14) 1041-60. Journal code: 9102074. ISSN: 1170-229X.

PUB. COUNTRY: New Zealand

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20031230
Last Updated on STN: 20031230

AB **Glucosamine** occurs naturally in all human tissues. It stimulates the synthesis of glycosaminoglycan, proteoglycan and **hyaluronic** acid, although the precise mechanism of action remains to be established. Formulated as **glucosamine** sulphate (Dona) and various others), **glucosamine** has been evaluated for its efficacy in relieving the symptoms of osteoarthritis and its disease-modifying potential.In two large randomised, double-blind, multicentre studies in patients with osteoarthritis, oral or intramuscular **glucosamine** for 4-6 weeks was associated with a greater decrease in symptom severity (as assessed by the Lequesne index) than placebo. In addition, there was a greater proportion of responders (defined as patients with a >or=3-point reduction in the Lequesne index, along with a positive overall assessment by the investigator) at the end of the treatment period with **glucosamine** than with placebo. In two large 4-week trials, oral **glucosamine** produced similar improvements to ibuprofen in the Lequesne index in one study and in articular pain scores in the other study. In a smaller 8-week comparative trial, oral **glucosamine** therapy achieved a significantly greater improvement in articular pain score than ibuprofen, and the investigators rated treatment efficacy as 'good' in a significantly greater proportion of **glucosamine** than ibuprofen recipients. In comparison with piroxicam, **glucosamine** significantly improved arthritic symptoms after 12 weeks of therapy and remained effective 8 weeks after treatment was discontinued. Beneficial effects of long-term oral **glucosamine therapy** in **preventing** joint space narrowing and improving symptoms were shown in two 3-year placebo-controlled trials in a total of 414 patients with **osteoarthritis**. Statistically significant differences favouring **glucosamine** were noted in the per-protocol and intention-to-treat analyses for the primary endpoints for both joint structural changes and symptom modification. **Glucosamine** has a tolerability profile similar to that of placebo and is better tolerated than ibuprofen or piroxicam. In particular, **glucosamine** recipients had a markedly lower incidence of gastrointestinal disturbances than those receiving ibuprofen. Other adverse events reported in both **glucosamine** and ibuprofen recipients were pruritus or skin reactions, flushing and fatigue. In general, a lower incidence of withdrawal from clinical trials was reported for **glucosamine** recipients than either ibuprofen or piroxicam recipients.CONCLUSION: In short-term clinical trials, **glucosamine** provided effective symptomatic relief for patients with osteoarthritis of the knee. In addition, **glucosamine** has shown promising results in modifying the progression of arthritis over a 3-year period. **Glucosamine** may therefore prove to be a useful **treatment** option for **osteoarthritis**.

L21 ANSWER 6 OF 40 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003416050 MEDLINE
DOCUMENT NUMBER: 22836247 PubMed ID: 12954956
TITLE: Intra-articular therapy in osteoarthritis.
AUTHOR: Uthman I; Raynauld J-P; Haraoui B
CORPORATE SOURCE: Department of Internal Medicine, Faculty of Medicine,

American University of Beirut, Beirut, Lebanon..
iuthman@aub.edu.lb
SOURCE: POSTGRADUATE MEDICAL JOURNAL, (2003 Aug) 79 (934) 449-53. Ref: 78
Journal code: 0234135. ISSN: 0032-5473.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030905
Last Updated on STN: 20031105
Entered Medline: 20031104

AB The medical literature was reviewed from 1968-2002 using Medline and the key words "intra-articular" and "**osteoarthritis**" to determine the various intra-articular **therapies** used in the **treatment** of **osteoarthritis**.
Corticosteroids and **hyaluronic** acid are the most frequently used intra-articular **therapies** in **osteoarthritis**. Other intra-articular substances such as orgotein, radiation synovectomy, dextrose prolotherapy, silicone, saline lavage, saline injection without lavage, analgesic agents, non-steroidal anti-inflammatory drugs, **glucosamine**, somatostatin, sodium pentosan polysulfate, chloroquine, mucopolysaccharide polysulfuric acid ester, lactic acid solution, and thiotepa cytostatica have been investigated as potentially therapeutic in the treatment of arthritic joints. Despite the lack of strong, convincing, and reproducible evidence that any of the intra-articular **therapies** significantly alters the progression of **osteoarthritis**, corticosteroids and **hyaluronic** acid are widely used in patients who have failed other **therapeutic** modalities for lack of efficacy or toxicity. As a practical approach for a knee with effusion, steroid injections should be considered while the presence of symptomatic "dry" knees may favour the **hyaluronic** acid approach. The virtual absence of serious side effects, coupled with the perceived benefits, make these approaches attractive.

L21 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 3

ACCESSION NUMBER: 2003:583865 BIOSIS
DOCUMENT NUMBER: PREV200300585593
TITLE: Radiological, arthroscopical evaluation and synovial membrane histology of the knee of dogs treated with chondroitin sulphate-sodium hialuronate association after experimental degenerative joint disease.
Original Title: Avaliacao radiologica e artroscopica e histologia da membrana sinovial do joelho de caes tratados com associacao de sulfato de condroitina e hialuronato de sodio, apos doenca articular degenerativa induzida experimentalmente..
AUTHOR(S): Arias S., S. A.; Rezende, C. M. F. [Reprint Author]; Melo, E. G.; Nunes, V. A.; Correa, J. C.
CORPORATE SOURCE: Departamento de Clinica e Cirurgia Veterinaria da Escola de Veterinaria, UFMG, 30123-970, Caixa Postal 567, Belo Horizonte, MG, Brazil

cleuza@dedalus.lcc.ufmg.br
SOURCE: Arquivo Brasileiro de Medicina Veterinaria e Zootecnia, (Agosto 2003) Vol. 55, No. 4, pp. 421-429. print.
ISSN: 0102-0935 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: Portuguese
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB The aim of this study was the assessment of **hyaluronic** acid and **chondroitin sulphate** association in the **therapy** of **degenerative joint disease** (DJD) in dogs. Ten mongrel dogs underwent arthroscopic section of cruciate cranial ligament aiming the development of DJD. Twenty one days after the procedure, surgical substitution of cruciate cranial ligament was carried out in all animals. Then five animals were treated with the combination of **hyaluronic** acid and **chondroitin sulphate** . The other five dogs were used as controls. Arthroscopical and radiological evaluations of the left fore limb were carried out before arthroscopic section at the some day and 90 days after cruciate cranial ligament substitution. Histologically the effect of the association of **hyaluronic** acid and **chondroitin sulphate** was more evident in the synovial membrane that had regeneration of the intimal layer and reduced lympho-plasmocitic infiltrate in the sub-intimal layer. However, the treatment did not prevent DJD cartilage lesions evaluated by arthroscopy and radiology.

L21 ANSWER 8 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:285754 SCISEARCH
THE GENUINE ARTICLE: BW36V
TITLE: Various interactions of drugs with cross-linked hyaluronate gel
AUTHOR: Yomota C (Reprint); Okada S
CORPORATE SOURCE: Natl Inst Hlth Sci Osaka, Chuo Ku, Hoenzaka 1-1-43, Osaka 5400006, Japan (Reprint); Natl Inst Hlth Sci Osaka, Chuo Ku, Osaka 5400006, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: POLYMER GELS: FUNDAMENTALS AND APPLICATIONS, (MAR 2003) Vol. 833, pp. 326-338.
Publisher: AMER CHEMICAL SOC, 1155 SIXTEENTH ST NW, WASHINGTON, DC 20036 USA.
ISSN: 0097-6156.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 18
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB **Hyaluronate**(**HA**) is a biopolymer composed of repeating disaccharide subunits of **N-acetyl**-D-**glucosamine** and D-glucuronate. HA is extensively distributed in connective tissue, synovial fluid of joints and in vitreous humor of the eye. It has been extensively used as a **therapeutic** agent in **osteoarthritis** and ophthalmic surgery. Thus hyaluronate is one of the natural polymers successfully applicable to the biomedical use. The basic properties of crosslinked HA gel have been reported(I) and there are several reports of applying the HA gel to medical devices(2,3). However it is reported that due to

the high swelling, the ability of the HA gel to retain other substances is not strong enough to use as a pharmaceutical reservoir(2).

Previously we noted the reports that some anionic polymer gels bind cationic surfactants(4,5). We have already reported that dodecyltrimethylammonium bromide(DOTMA) binds HA in solution cooperatively and that the binding constant is much smaller than those of other anionic polysaccharides such as **chondroitin sulfate**(6). Furthermore the crosslinked HA gel was observed to shrink with time in addition of DOTMA, and the weight of the gel decreased by only 2-4% of the initial weight(7). On the other hand, it is well known that many kinds of drugs have properties of surfactants, and self association (micelle) in aqueous solution have been investigated(8-13). Therefore as cationic surfactants, some drugs were expected to cause the shrinking of the HA gel. The interactions of the crosslinked HA gel with several kinds of cationic drugs were investigated, and the release of incorporated substances was measured. (C) 2003 American Chemical Society.

L21 ANSWER 9 OF 40 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4

ACCESSION NUMBER: 2003:523970 BIOSIS
DOCUMENT NUMBER: PREV200300526101
TITLE: Drug therapy: Only symptomatic or also causal treatment?.
Original Title: Medikamentoese Therapie: Nur symptomatische oder auch kausale Behandlung?.
AUTHOR(S): Bach, G. L. [Reprint Author]; Foerster, K. K.
CORPORATE SOURCE: Innere Medizin/Rheumatologie, Beim Bergtor 12, 67269, Gruenstadt, Germany
GerhardLBach@yahoo.de
SOURCE: Deutsche Zeitschrift fuer Sportmedizin, (Juni 2003) Vol. 54, No. 6, pp. 199-204. print.
ISSN: 0344-5925 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: German
ENTRY DATE: Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

AB Osteoarthritis is a degenerative joint disease of the hyalin cartilage of synovial joints. Clinically the disease is characterized by joint pain, tenderness, limitation of movement, occasional effusions, and local inflammation of various extent. Therefore, the reduction of inflammation and alleviation of pain are goals of primary conservative treatment. This treatment is purely symptomatic as monotherapy or as a combined treatment involving physical, orthopedic and medical measures. In 1996, increasing interest in a causal drug **therapy** to **osteoarthritis** led to the classification of "symptom-modifying" and "structure-modifying" drugs. Pure analgesics, classical non-steroidal anti-inflammatory drugs (NSAIDs) - non-selective and COX-2-selective as well-, intraarticular corticosteroids and other pharmacological agents were classified as "symptom-modifying". **Glucosamine** sulfate and **hyaluronic** acid also belong to this group. Both substances have been shown to act as "symptom-modifying" agents. In addition studies indicate a clinically relevant "structure-modification" with a potential to inhibit the progress of osteoarthritis over a long-term. In the future prospective, randomized studies are needed

to evaluate various kinds of medical treatment for the potential of having symptom- and structure-modifying effect.

L21 ANSWER 10 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 5

ACCESSION NUMBER: 2003293984 EMBASE
TITLE: Pharmacologic treatment alternatives.
AUTHOR: Nolte R.M.; Klimkiewicz J.J.
CORPORATE SOURCE: Dr. J.J. Klimkiewicz, Department of Orthopaedic Surgery, Division of Sports Medicine, Georgetown University Medical Center, Washington, DC, United States. kajklim@pol.net
SOURCE: Sports Medicine and Arthroscopy Review, (2003) 11/2 (102-106).
Refs: 26
ISSN: 1062-8592 CODEN: SMARCV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Before consideration of the surgical alternatives for **osteoarthritis**, traditional **therapy** has focused on the symptomatic management of this disease process. Recently, a new conservative alternative has gained popularity in attempting to modify and even reverse the breakdown of articular cartilage in this condition. These disease-modifying agents include the nutricueticals chondroitin and **glucosamine** sulfate, in addition to the viscosupplements, containing **hyaluronic** acid. This review acts as updated review on the conservative management of **osteoarthritis**.

L21 ANSWER 11 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003392410 EMBASE
TITLE: Management of the arthritic knee in older people.
AUTHOR: Dervin G.F.
CORPORATE SOURCE: Dr. G.F. Dervin, University of Ottawa, Ottawa Hospital, Orthopaedic Division, Ottawa, Ont., Canada
SOURCE: Geriatrics and Aging, (1 Sep 2003) 6/8 (20-24).
Refs: 29
ISSN: 1488-8408 CODEN: GAEGB5
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
027 Biophysics, Bioengineering and Medical Instrumentation
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Understanding the options for **treatment** of **osteoarthritis** of the knee will allow physicians to help

their patients realize the physical and social demands of healthy life. Weight loss,physical **therapy** and unloading braces are clinically proven strategies in the early stages of the disease. Acetaminophen remains the analgesic of choice, while COX-2 NSAIDs are reserved for flare-ups and short-term use. Oral **glucosamine** and **chondroitin sulfate** also may be helpful. Persistently swollen knees may respond to aspiration and corticosteroid injection or viscosupplementation with **hyaluronic** acid derivatives. Those with acute onset of mechanical symptoms may respond to arthroscopic debridement and resection of unstable meniscal tears. Osteotomy of the tibia or femur are options for isolated unicompartmental disease in younger and more active patients. Arthroplasty of one or all compartments of the knee is the definitive procedure for end-stage arthrosis with very dependable results in most clinical settings.

L21 ANSWER 12 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-617109 [66] WPIDS
DOC. NO. CPI: C2002-174439
TITLE: Chondroprotective/restorative composition useful for treating or preventing osteoarthritis and other joint diseases in mammals comprises hyaluronic acid or its salts.
DERWENT CLASS: A96 B05 C03 D13
INVENTOR(S): PIERCE, S W
PATENT ASSIGNEE(S): (PIER-I) PIERCE S W
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2002068718 | A1 | 20020606 | (200266)* | | 14 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 2002068718 | A1 Provisional | US 2000-237838P | 20001003 |
| | | US 2001-967977 | 20011002 |

PRIORITY APPLN. INFO: US 2000-237838P 20001003; US 2001-967977 20011002
AN 2002-617109 [66] WPIDS
AB US2002068718 A UPAB: 20021014
NOVELTY - A chondroprotective/restorative composition comprises **hyaluronic** acid or its salts and optionally a pharmaceutical carrier.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of **treating** or **preventing** **osteoarthritis**, joint effusion, joint inflammation and pain, synovitis, lameness, post operative arthroscopic surgery, deterioration of proper joint function, reduction or inhibition of metabolic activity of chondrocytes, activity of enzymes that degrade cartilage, reduction or inhibition of production of **hyaluronic** acid in mammals comprises oral administration of **hyaluronic** acid or its salt;

(2) an animal feed having chondroprotective/restorative benefits comprising a nutritionally effective feed base selected from grains, proteins, and/or fats, and an **hyaluronic** acid or its salts; and

(3) a therapeutic and chondroprotective/restorative composition comprising **Hyaluronic** acid or its salts, a therapeutic drug, and optionally a pharmaceutical carrier.

ACTIVITY - Osteopathic; Antiarthritic; Anti-inflammatory; Analgesic.

MECHANISM OF ACTION - None given.

USE - Fort **treating** or **preventing** **osteoarthritis**, joint effusion, joint inflammation and pain, synovitis, lameness, post operative arthroscopic surgery, deterioration of proper joint function, reduction or inhibition of metabolic activity of chondrocytes, activity of enzymes that degrade cartilage, reduction or inhibition of production of **hyaluronic** acid in mammals. **Hyaluronic** acid, optionally in combination with **glucosamine** sulfate and/or **chondroitin sulfate** is useful in chondroprotective/restorative compositions. The composition is useful in an animal feed comprising a feed base selected from grains, proteins, fats and mixtures of these. The animal feed further includes molasses. The animal feed is in the form of a paste and is a cat, dog or horse feed.

Dwg.0/0

L21 ANSWER 13 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-427934 [46] WPIDS
DOC. NO. CPI: C2002-121539
TITLE: Medicament for treating osteoarthritis by intraarticular injection, containing plasma as synovial fluid replacement, preferably together with pentosan polysulfate, alpha-tocopherol and phospholipid.
DERWENT CLASS: B04
PATENT ASSIGNEE(S): (KIEF-I) KIEF H
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| DE 10054257 | A1 | 20020516 | (200246)* | | 4 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| DE 10054257 | A1 | DE 2000-10054257 | 20001102 |

PRIORITY APPLN. INFO: DE 2000-10054257 20001102
AN 2002-427934 [46] WPIDS
AB DE 10054257 A UPAB: 20020722
NOVELTY - A medicament (I) for intraarticular injection contains body-compatible plasma, recovered from blood after induction of a coagulation process, as replacement for missing synovial fluid.

ACTIVITY - Antiarthritic; Osteopathic; Antiinflammatory.

No suitable biological data given.

MECHANISM OF ACTION - Synovial fluid substitute for stimulating cartilage metabolism.

USE - (A) is useful for **treating osteoarthritis**, by replacing the protein component of synovial fluid, stimulating cartilage metabolism (due to the activated oxygen content of the plasma), alleviating proteoglycan (e.g. **hyaluronic** acid and **chondroitin sulfate**) deficiency and controlling inflammation.

ADVANTAGE - (I) markedly improves the moveability and reduces the pain in joints affected by osteoarthritis, for a period of months or even years. The combination of lipid- and water-soluble components provides an amphoteric base with a depot effect. (I) is obtainable as a homogeneous, clear solution which is easy to handle and inject into joint cavities.

Dwg.0/1

L21 ANSWER 14 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002152257 EMBASE

TITLE: Hyaluronan increases glomerular cyclooxygenase-2 protein expression in a p38 MAP-kinase-dependent process.

AUTHOR: Dunlop M.E.; Muggli E.E.

CORPORATE SOURCE: Dr. M.E. Dunlop, University of Melbourne, Department of Medicine, Royal Melbourne Hospital, Grattan Street, Parkville, Vic. 3050, Australia. medunlop@unimelb.edu.au

SOURCE: Kidney International, (2002) 61/5 (1729-1738). Refs: 66
ISSN: 0085-2538 CODEN: KDYIA5

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background. Accumulation of the matrix glycosaminoglycan **hyaluronan** occurs in many types of renal injury but could follow any provision of **hyaluronan** substrate to the kidney, for example, through widespread use of supplementary **glucosamine** in **osteoarthritic** conditions. **Hyaluronan** can increase cyclooxygenase-2 (COX-2) protein and prostaglandin production. This effect was characterized in rat renal glomeruli to determine the cellular mechanism of activation. Methods. Isolated glomeruli were **treated** with purified **hyaluronan** (molecular mass 2 x 10(5) D) for up to 24 hours. Results. An increase in cyclooxygenase capacity and COX-2 protein was shown to follow the activation of p38-mitogen-activated protein (MAP) kinase and to be inhibited by a specific pyridinyl imadazole inhibitor (SB 202190). **Hyaluronan**-induced activation of cytosolic phospholipase A2 also was shown to be a p38 MAP kinase effect in these preparations. Prostaglandin production was inhibited by COX-2-specific non-steroidal anti-inflammatory compounds (NS-398 and celecoxib) but, as shown for many non-steroidal anti-inflammatory drugs (NSAIDs), an increase in COX-2 protein accompanied this inhibition. Conclusions. We propose that these

findings have clinical relevance. Prostaglandins have a number of important intrarenal regulatory effects leading to some debate over renal function with the use of NSAIDs. Where **hyaluronan** is increased, p38 MAP-kinase-dependent provision of prostaglandin substrate, via activation of cytosolic phospholipase A2, and a concomitant increase in cyclooxygenase-2 protein would raise renal prostaglandin levels. While NSAID **treatment** can **prevent** a rise in prostaglandin levels, it needs to be maintained to avoid possible exacerbation of pro-inflammatory conditions due to increased COX-2 protein levels.

L21 ANSWER 15 OF 40 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002701312 MEDLINE
DOCUMENT NUMBER: 22348633 PubMed ID: 12462019
TITLE: A comparison of the efficacy of conservative therapies for obese patients with osteoarthritis of the knee.
AUTHOR: Toda Yoshitaka
CORPORATE SOURCE: Kishoukai Toda Orthopedic Rheumatology Clinic, Toyotsu-cho, Suita-city.
SOURCE: RYUMACHI, (2002 Oct) 42 (5) 795-800.
Journal code: 0153217. ISSN: 0300-9157.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030123
Entered Medline: 20030122

AB Two hundred and five obese women with **osteoarthritis** of the knee (knee OA) were **treated** with one of the following interventions for six weeks: A nonsteroidal anti-inflammatory drug (NSAID) alone (Control, n = 16), NSAID combined with walking (n = 16), NSAID with non-weight bearing exercises (n = 16), NSAID with intra-articular **hyaluronan** injections (NH, n = 16), NSAID with supplement foods, **glucosamine** and condroitin (NS, n = 15), traditional shoe inserts, wedged insoles (NT, n = 20), NSAID with a novel insole with an elastic subtalar strapping (NN, n = 25), an energy restriction diet plus the NSAID (ND, n = 32), a diet combined with the NSAID and exercises (NDE, n = 25), and the diet combined with the NSAID and walking (NDW, n = 24). The Lequesne index was employed to obtain remission percentages, which were then compared between the ten groups. Compared with all but the NDW group, the NDE group showed a significant improvement. The NDW group also demonstrated a significant improvement, compared with all but the NDE and NN groups. The NN group showed a significant improvement compared with the control, NS and ND groups. However, for patients in the NDE and NDW groups, it was difficult to maintain body composition, even with these intervention methods. In this regard, the use of the insole with the elastic subtalar strapping was a simple and convenient method to maintain the body composition effect of the intervention method for knee OA patients.

L21 ANSWER 16 OF 40 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002434287 MEDLINE
DOCUMENT NUMBER: 22178657 PubMed ID: 12192262
TITLE: Oral and intra-articular remedies: Review of papers

published from March 2001 to February 2002.
AUTHOR: Jubb Ronald W
CORPORATE SOURCE: University of Birmingham, Selly Oak Hospital, UK.. Ronald.jubb@uhb.nhs.uk
SOURCE: CURRENT OPINION IN RHEUMATOLOGY, (2002 Sep) 14 (5) 597-602. Ref: 45
Journal code: 9000851. ISSN: 1040-8711.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020823
Last Updated on STN: 20030129
Entered Medline: 20030128

AB There have been considerable advances in the drug **treatments** used to **treat osteoarthritis**. The development of selective cyclo-oxygenase inhibitors (COX-II) and confirmation of their efficacy and gastrointestinal safety will reduce treatment morbidity in the elderly. Guidelines for safe and appropriate use of COX-II drugs are now available. The role of anti-inflammatory drugs in precipitating cardiorenal events has been highlighted but remains to be fully evaluated. **Glucosamine**, diacerein, and **hyaluronan** may all be disease-modifying drugs for osteoarthritis but confirmatory studies are still needed.

L21 ANSWER 17 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 8
ACCESSION NUMBER: 2002182693 EMBASE
TITLE: [Intraarticular Hyaluronic acid in osteoarthritis of the carpometacarpal joint].
INTRA-ARTIKULARE HYALURONSAIURE BEI DER ARTHROSE DES DAUMENSATTELGELENKS.
AUTHOR: Talke M.
CORPORATE SOURCE: Dr. M. Talke, Arzt fur Orthopadie, Klosterstrasse 34-35, 13581 Berlin, Germany
SOURCE: Aktuelle Rheumatologie, (2002) 27/2 (101-106).
Refs: 14
ISSN: 0341-051X CODEN: AKRHDB
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB **Osteoarthritis** (OA) of the carpometacarpal (CMC) joint is a very common problem in elderly patients. In a survey, 30% out of 25000 patients suffering from OA reported problems located in the CMC joint while, in an epidemiological study, 53% of women between 75 and 79 years of age showed signs of OA of the CMC joint. Pain and degeneration of joint structures may adversely affect joint function and the quality of life in such patients. Current conservative **treatment** includes physiotherapy followed by the topical and oral administration of analgesics and non-steroidal antirheumatic drugs and intra-articular (i.a.) glucocorticoids respectively. This

is the first report on the safety and efficacy of i.a. exogenous **Hyaluronic** acid (**HA**) in patients with OA of the CMC joint. Endogenous HA, a biopolymer made up of repeating sequences of N-**acetylglucosamine** and glucuronic acid, plays a crucial role in the structure, function and pathology of synovial joints: HA forms part of the cartilage matrix. It also coats the surface of the cartilage and the synovial membrane and confers viscoelasticity to the synovial fluid. In OA, the quality and quantity of endogenous HA in the joint is reduced and numerous clinical studies have shown the **therapeutic** value of using exogenous HA in OA of bigger joints, such as the knee joint. Twenty patients suffering from severe pain due to radiologically ascertained OA of the CMC joint, were included in an open, prospective clinical study. **Treatment** consisted of two to three i.a. injections of 10 mg/1 ml HA, obtained by fermentation (Ostenil mini, a presentation specifically developed for **treatment** of smaller joints), which were administered at weekly intervals. The efficacy parameters were pain, assessed using a Huskisson Visual Analogue Scale (VAS), grip strength (pulp pinch and lateral pinch) assessed using an intrinsicmeter, joint mobility, crepitation during passive movement of the joint and the global clinical impression of investigator and patients. Safety was assessed by the documentation of clinically evident adverse events. The time sequence of the assessments, with a final evaluation of all patients three months after the end of the i.a. **treatment**, allowed to differentiate between the "immediate" effects and the "carry over" effects of i.a. HA. A marked reduction of pain (from 63.95 ± 11.06 to 39.30 ± 13.24 mm VAS, -38.55%) and an increase in grip strength (pulp pinch: 1.48 ± 0.52 to 2.09 ± 0.90 grades, ± 37.84%; lateral pinch: 2.10 ± 0.74 to 2.87 ± 1.01 grades, 36.67%) was observed when the pre-**treatment** values were compared to those obtained at the end of the observation period. These differences reached statistical significance ($p < 0.001$, Friedman test). Crepitation persisted in only three out of eleven patients while joint mobility on radial and palmar abduction also showed a marked improvement. In 19 out of the 20 cases, the investigator and patients were satisfied with the improvements in signs and symptoms achieved in this study. Considering that no adverse effects were reported, the benefit-risk-evaluation favours the use of i.a. HA in this indication. It can be concluded that i.a. HA is a promising new option in the **treatment** of OA of the CMC joint. The findings of this study should be confirmed in controlled clinical studies with a longer observation period.

L21 ANSWER 18 OF 40 MEDLINE on STN
ACCESSION NUMBER: 2002101869 MEDLINE
DOCUMENT NUMBER: 21820886 PubMed ID: 11833521
TITLE: Meeting the therapeutic challenge of the patient with osteoarthritis.
AUTHOR: Todd Cathryn
CORPORATE SOURCE: Rocky Mountain Poison Control and Drug Consultation Center, Denver, Colo, USA.. scarab@rmi.net
SOURCE: JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, (2002 Jan-Feb) 42 (1) 74-82. Ref: 90
Journal code: 9601004. ISSN: 1086-5802.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

Searcher : Shears 571-272-2528

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020209
Last Updated on STN: 20020315
Entered Medline: 20020314

AB OBJECTIVE: To discuss the diagnosis of **osteoarthritis** and the efficacy of available pharmacologic and nonpharmacologic **treatment** options. DATA SOURCES: Published reports on the diagnosis and **treatment** of **osteoarthritis** were identified through a MEDLINE search of English-language journal articles using a focused title search for the keywords acetaminophen, nonsteroidal anti-inflammatory, COX-2 nonsteroidal, opioids, capsaicin, tramadol, **glucosamine**, **hyaluronic** acid, and **osteoarthritis** and by reviewing the bibliographies of selected reviews. The American College of Rheumatology (ACR) guidelines, as updated in September 2000, for the **treatment** of **osteoarthritis** of the hip and knee were analyzed with appropriate references to clinical and scientific studies, review articles, and other published guidelines. DATA SYNTHESIS: Each patient's medical history and level of pain should decide the most appropriate treatment. Nonpharmacologic therapies should always be included in the treatment regimen. If further pain management is required, the most appropriate pharmacologic treatments are acetaminophen or nonsteroidal anti-inflammatory drugs for mild-to-moderate pain, tramadol or opioid combinations for moderate-to-moderately severe pain, and opioids for severe pain. Adjunctive treatments, intraarticular injections, and surgery are also viable options for some patients. CONCLUSION: If used properly, the ACR guidelines for the **treatment** of **osteoarthritis** are important tools in the care of the patient with this disease.

L21 ANSWER 19 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001183943 EMBASE
TITLE: Effects of high molecular weight hyaluronan on the distribution and movement of proteoglycan around chondrocytes cultured in alginate beads.
AUTHOR: Kikuchi T.; Yamada H.; Fujikawa K.
CORPORATE SOURCE: H. Yamada, Department of Orthopaedic Surgery, Fujita Health University, Second Hospital, 3-6-10 Otobashi, Nakagawaku, Nagoya 454-8509, Japan. hayamada@fujita-hu.ac.jp
SOURCE: Osteoarthritis and Cartilage, (2001) 9/4 (351-356). Refs: 31
ISSN: 1063-4584 CODEN: OSCAEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To evaluate the effects of high molecular weight **hyaluronan** (**HA**) on the distribution and movement of proteoglycan (PG) formed around rabbit chondrocytes cultured in

alginate beads. Design: Rooster comb-derived HA (MW 8x10(5) Da) was co-polymerized in alginate gel to study the direct effects of extrinsic HA on chondrocytes. PG metabolism of rabbit chondrocytes cultured in alginate beads was examined by measuring the incorporation of [(35)S]sulfate into glycosaminoglycan in two distinct regions, the cells with their cell-associated matrix (CM) and the further-removed matrix (FRM). Immunohistochemical analysis was performed using monoclonal antibodies against **chondroitin sulfate** and keratan sulfate. Autoradiography using degenerated cartilage tissue from the rabbit **osteoarthritis** (OA) model was performed to discover the effect of HA on the distribution of newly-synthesized PG in the cartilage tissue. Results: The incorporation of [(35)S]sulfate into newly-synthesized PG in the cells with CM decreased with the addition of 0.125-1.0 mg/ml HA, while the incorporation in the FRM increased. These effects of HA on the distribution of newly-synthesized PG were the same either in chondrocytes with CM or chondrocytes without CM. Immunohistochemical analysis showed that staining of PG in the CM was decreased and staining in the FRM was increased in the HA **treated** group compared to the control group. Autoradiography using degenerated cartilage tissue from the rabbit OA model indicated that [(35)S]-labeled macromolecules showed a more diffuse distribution in the HA **treated** group compared with the control group. Conclusion: These results indicate that extrinsic HA could affect the movement of newly-synthesized PG from the CM to the FRM in both alginate beads and cartilage tissue. 

L21 ANSWER 20 OF 40 MEDLINE on STN DUPLICATE 9

| | |
|---|---|
| ACCESSION NUMBER: | 2002069912 MEDLINE |
| DOCUMENT NUMBER: | 21653857 PubMed ID: 11795556 |
| TITLE: | Pharmacological therapies for the treatment of osteoarthritis. |
| AUTHOR: | McColl G J |
| CORPORATE SOURCE: | Centre for Rheumatic Diseases, Royal Melbourne Hospital, Parkville, VIC.. g.mccoll@medicine.unimelb.edu.au |
| SOURCE: | MEDICAL JOURNAL OF AUSTRALIA, (2001 Nov 19) 175 Suppl S108-11. Ref: 30 Journal code: 0400714. ISSN: 0025-729X. |
| PUB. COUNTRY: | Australia |
| DOCUMENT TYPE: | Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW) (REVIEW, TUTORIAL) |
| LANGUAGE: | English |
| FILE SEGMENT: | Priority Journals |
| ENTRY MONTH: | 200202 |
| ENTRY DATE: | Entered STN: 20020125 Last Updated on STN: 20020202 Entered Medline: 20020201 |

AB Non-pharmacological interventions are the first-line **therapy** for **osteoarthritis**. If non-pharmacological therapy fails, paracetamol (up to 4 g daily) should be added. If paracetamol fails, the patient's risk factors for gastrointestinal and renal disease should be assessed. In patients with gastrointestinal risk factors, a COX-2-specific inhibitor (CSI) would be used in preference to a conventional non-steroidal anti-inflammatory drug

(NSAID). In patients with renal risk factors, NSAIDs and CSIs should be used with care. In patients who continue to have problems, other treatments should be considered; these might include intra-articular **hyaluronan** or depot corticosteroid, analgesia or **glucosamine**.

L21 ANSWER 21 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-061650 [07] WPIDS
DOC. NO. CPI: C2001-017150
TITLE: Herbal compositions comprising glucosamine and Tripterygium wilfordii, Ligustrum lucidum and/or Erycibe schmidtii, for treating inflammation or degeneration of joint tissues, e.g. arthritis.
DERWENT CLASS: B04 C03 D13
INVENTOR(S): BABISH, J G; YU, H; ZHONG, S
PATENT ASSIGNEE(S): (OXFO-N) OXFORD NATURAL PROD PLC
COUNTRY COUNT: 94
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2000074696 | A1 | 20001214 | (200107)* | EN | 20 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000052310 | A | 20001228 | (200119) | | |
| EP 1185281 | A1 | 20020313 | (200225) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | | | |
| GB 2367492 | A | 20020410 | (200232) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000074696 | A1 | WO 2000-GB2092 | 20000601 |
| AU 2000052310 | A | AU 2000-52310 | 20000601 |
| EP 1185281 | A1 | EP 2000-937014 | 20000601 |
| | | WO 2000-GB2092 | 20000601 |
| GB 2367492 | A | WO 2000-GB2092 | 20000601 |
| | | GB 2001-31054 | 20011228 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2000052310 | A | Based on | WO 2000074696 |
| EP 1185281 | A1 | Based on | WO 2000074696 |
| GB 2367492 | A | Based on | WO 2000074696 |

PRIORITY APPLN. INFO: US 1999-153977P 19990914; US 1999-137172P 19990602
AN 2001-061650 [07] WPIDS
AB WO 200074696 A UPAB: 20011129

NOVELTY - Herbal composition comprising **glucosamine** and at least one herb which is Tripterygium wilfordii, Ligustrum lucidum or Erycibe schmidtii, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a food product comprising the composition.

ACTIVITY - Antiinflammatory; osteopathic; antiarthritic; antirheumatic.

Tablets were prepared comprising 21 mg/kg **glucosamine**, 1.5 mg/kg Tripterygium wilfordii extract (0.1 weight% triptolide), 5.0 mg/kg Ligustrum lucidum extract (45% oleanolic acid) and 6.5 mg/kg Erycibe schmidtii extract (0.35% scopoletin) with tabletting excipients. In a clinical study carried out on dogs, the tablet dosage form was administered daily to a group of dogs (1 tablet/day) suffering from arthritis. Preliminary observations by a veterinarian after 7-10 days indicated that there was an improvement in each animal's condition.

MECHANISM OF ACTION - Enhances synthesis of gucosaminoglycans and **hyaluronic** acid.

USE - For **treating** inflammation or degeneration of joint tissues, e.g. arthritis, particularly rheumatoid arthritis or **osteoarthritis**. The composition may be formulated as a dietary supplement or pharmaceutical or veterinary composition (e.g. for **treating** dogs, cats, horses or cattle).

**Glucosamine** diminishes tissue destruction, Tripterygium wilfordii inhibits expression of cyclooxygenase-2 (COX-2) mRNA, Ligustrum lucidum inhibits COX-2 enzyme activity and Erycibe schmidtii can inhibit inflammation and relieve pain.

ADVANTAGE - The composition is suitable for reducing inflammatory responses without having harmful side effects. Combining **glucosamine** with the Chinese herbs provides improved treatment of pain and inflammation not possible with **glucosamine** alone and reduces the need to use steroidal antiinflammatory drugs which can cause damage to the gastrointestinal system over extended periods of time.

Dwg.0/1

L21 ANSWER 22 OF 40 MEDLINE on STN DUPLICATE 10

| | |
|---|---|
| ACCESSION NUMBER: | 2000318851 MEDLINE |
| DOCUMENT NUMBER: | 20318851 PubMed ID: 10859690 |
| TITLE: | Sulfated glycosaminoglycans and glucosamine may synergize in promoting synovial hyaluronic acid synthesis. |
| AUTHOR: | McCarty M F; Russell A L; Seed M P |
| CORPORATE SOURCE: | NutriGuard Research, La Jolla, CA, USA. |
| SOURCE: | MEDICAL HYPOTHESES, (2000 May) 54 (5) 798-802. Journal code: 7505668. ISSN: 0306-9877. |
| PUB. COUNTRY: | SCOTLAND: United Kingdom |
| DOCUMENT TYPE: | Journal; Article; (JOURNAL ARTICLE) |
| LANGUAGE: | English |
| FILE SEGMENT: | Priority Journals |
| ENTRY MONTH: | 200007 |
| ENTRY DATE: | Entered STN: 20000728<br>Last Updated on STN: 20000728<br>Entered Medline: 20000720 |

AB High-molecular-weight **hyaluronic** acid (**HA**) produced by the synovium may function physiologically to aid preservation of cartilage structure and **prevent** arthritic pain; both the size and concentration of HA in synovial fluid are

diminished in **osteoarthritis** (OA). **Glucosamine** therapy for OA can be expected to increase synovial HA production by providing rate-limiting substrate. In addition, certain sulfated glycosaminoglycans and polysaccharides - including **chondroitin sulfate** (CS), dermatan sulfate, and pentosan polysulfate - stimulate synovial HA production, apparently owing to a hormone-like effect triggered by the binding of these polymers to membrane proteins of synovial cells. Surprisingly, a significant proportion of orally administered CS is absorbed as intact polymers - apparently by pinocytosis. These considerations may rationalize clinical studies concluding that oral CS provides slow-onset but durable pain relief and functional improvement in OA. The possibility that oral **glucosamine** and CS may interact in a complementary or synergistic fashion to improve synovial fluid HA content in OA should be assessed in clinical studies, and the potential of adjunctive CS administration to improve the clinical response achievable with optimal intakes of **glucosamine** should likewise be evaluated. In light of the fact that the synovium virtually functions as a 'placenta' for cartilage, focusing on synovium as the target for therapeutic intervention in OA may be a rational strategy.



L21 ANSWER 23 OF 40 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 2001204747 MEDLINE
DOCUMENT NUMBER: 21129938 PubMed ID: 11234282
TITLE: [Water-exchange processes in hyaline cartilage and its basic components in a normal state and in osteoarthritis].
Vlagoobmennye protsessy v gialinovom khriashche i ego osnovnykh komponentakh v norme i osteoartroze.
AUTHOR: Nikolaeva S S; Chkhol K Z; Bykov V A; Roshchina A A; Iakovleva L V; Koroleva O A; Omel'ianenko N P; Rebrov L B
CORPORATE SOURCE: Scientific Research and School-methodical Center for Biomedical Technology, 123056 Moscow, Krasina str. 2.
SOURCE: VOPROSY MEDITSINSKOI KHIMII, (2000 Nov-Dec) 46 (6) 581-90.
Journal code: 0416601. ISSN: 0042-8809.
PUB. COUNTRY: Russia: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010417
Last Updated on STN: 20010417
Entered Medline: 20010412

AB The content of different forms of tissue water was studied in the normal articular cartilage and osteoarthrosis cartilage and its structural components: collagen, potassium hyaluronate, sodium chondroitinsulphate and its complexes. In the components of cartilage matrix a few of fractions of bound water different in the strength of binding are present. At the maximal humidity, all water in collagen binds with the active groups of biopolymers and in the glycosaminoglycans, in addition to bound water, are present, two crystal forms of freezing water (free water) at least. The quantity of free water in the collagen-chondroitin sulphat membrane, is increased with the increase of **chondroitin**

**sulphate**. In the collagen-hyaluronate complex, fraction of free water is found only at the low concentration of hyaluronate kalium. It was shown that in the hyalin cartilage, in different from the other connective tissue (skin, achilles tendon), the most part of water is free water and its quantity is increased in the osteoarthrosis. It is supposed that the rearrangement of binding and free-water fractions in the **osteoarthrosis** is the result of deficiency of **hyaluronic** acid and therefore this may be regarded in the improvement of methods of **treatment** . This scientific and methodical approach allow to receive information on the forms and binding energy of water in the biological tissues, which is absorbed from fluids and steam phase and determine characters of the pathological changes.

L21 ANSWER 24 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:596539 SCISEARCH
THE GENUINE ARTICLE: 339VG
TITLE: Chondroprotective agents in the treatment of articular cartilage degeneration
AUTHOR: Tomford W W (Reprint)
CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, DEPT ORTHOPAED SURG, 55 FRUIT ST, BOSTON, MA 02114 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: OPERATIVE TECHNIQUES IN SPORTS MEDICINE, (APR 2000) Vol. 8, No. 2, pp. 120-121.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 1060-1872.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 10
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB **Glucosamine**, **chondroitin**. **sulfate**, and **hyaluronic** acid provide new and exciting **treatments** for **osteoarthritis**. Although the use of these drugs is still controversial, they have gained popularity among the lay public, suggesting that they may have beneficial effects. Studies are now being performed to test the effectiveness of these medicines and, in particular, whether they function simply as placebos. Knowledge of these **treatments** is important for orthopedists **treating** young patients with articular cartilage damage.

L21 ANSWER 25 OF 40 MEDLINE on STN
ACCESSION NUMBER: 2001502142 MEDLINE
DOCUMENT NUMBER: 21436910 PubMed ID: 11552610
TITLE: [News in the treatment of rheumatic diseases]. Novosti u lijecenju reumatskih bolesti.
AUTHOR: Babic-Naglic D
CORPORATE SOURCE: Klinika za reumatske bolesti i rehabilitaciju Medicinskoga fakulteta Sveucilista u Zagrebu KBC Zagreb, Zagreb.
SOURCE: REUMATIZAM, (2000) 47 (2) 20-4. Ref: 37
Journal code: 0216650. ISSN: 0374-1338.
PUB. COUNTRY: Croatia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)

LANGUAGE: Serbo-Croatian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010913
Last Updated on STN: 20011001
Entered Medline: 20010927

AB Rheumatic diseases are frustrating issue for the rheumatologists because ethiologic remedy is still missing and much more, they are great socio-economic burden for patients and society. In the last 10 years there was bustling endeavour in creating new products with exact known action. This article deal the new options to **treat** rheumatoid arthritis with leflunomide, infliximab, etanercept and anakinra and **osteoarthritis** with **hyaluronan**, diacerhein, glucosamino sulphate, **chondroitin sulphate** and avocado/soya unsaponifiables. In particular patients all mentioned products have their place in the treatment plan but critical risk-benefit assessment is needed.

L21 ANSWER 26 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 12
ACCESSION NUMBER: 1999395042 EMBASE
TITLE: Niacinamide therapy for osteoarthritis - Does it inhibit nitric oxide synthase induction by interleukin-1 in chondrocytes?.
AUTHOR: McCarty M.F.; Russell A.L.
CORPORATE SOURCE: Dr. M.F. McCarty, NutriGuard Research, 1051 Hermes Avenue, Encinitas, CA 92024, United States
SOURCE: Medical Hypotheses, (1999) 53/4 (350-360).
Refs: 157
ISSN: 0306-9877 CODEN: MEHYDY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Fifty years ago, Kaufman reported that high-dose niacinamide was beneficial in **osteoarthritis** (OA) and rheumatoid arthritis. A recent double-blind study confirms the efficacy of niacinamide in OA. It may be feasible to interpret this finding in the context of evidence that synovium-generated interleukin-1 (IL-1), by inducing nitric oxide (NO) synthase and thereby inhibiting chondrocyte synthesis of aggrecan and type II collagen, is crucial to the pathogenesis of OA. Niacinamide and other inhibitors of ADP-ribosylation have been shown to suppress cytokine-mediated induction of NO synthase in a number of types of cells; it is therefore reasonable to speculate that niacinamide will have a comparable effect in IL-1-exposed chondrocytes, blunting the anti-anabolic impact of IL-1. The chondroprotective antibiotic doxycycline may have a similar mechanism of action. Other nutrients reported to be useful in OA may likewise intervene in the activity or synthesis of IL-1. Supplemental **glucosamine** can be expected to stimulate synovial synthesis of **hyaluronic** acid; **hyaluronic** acid suppresses the anti-catabolic effect of IL-1 in chondrocyte cell cultures, and has documented **therapeutic** efficacy when injected intra-articularly.

S-adenosylmethionine (SAM), another proven **therapy** for OA, upregulates the proteoglycan synthesis of chondrocytes, perhaps because it functions physiologically as a signal of sulfur availability. IL-1 is likely to decrease SAM levels in chondrocytes; supplemental SAM may compensate for this deficit. Adequate selenium nutrition may down-regulate cytokine signaling, and ample intakes of fish oil can be expected to decrease synovial IL-1 production; these nutrients should receive further evaluation in OA. These considerations suggest that non-toxic nutritional regimens, by intervening at multiple points in the signal transduction pathways that promote the synthesis and mediate the activity of IL-1, may provide a substantially superior alternative to NSAIDs (merely palliative and often dangerously toxic) in the **treatment** and perhaps **prevention** of OA.

L21 ANSWER 27 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 13

ACCESSION NUMBER: 1999317699 EMBASE
TITLE: [The pharmacological basis of therapeutics in osteoarthritis].
PHARMAKOLOGISCHE GRUNDLAGEN DER ARTHROSETHERAPIE.
AUTHOR: Steinmeyer J.
CORPORATE SOURCE: Dr. J. Steinmeyer, Orthopadische Klinik, Med. Zentrum Orthopadie/Phys. Med., Justus-Liebig-Universitat Giessen, Paul-Mcimberg-Str. 3, D-35385 Giessen, Germany
SOURCE: Medizinische Welt, (1999) 50/8 (341-347).
Refs: 55
ISSN: 0025-8512 CODEN: MEWEAC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB This review summarizes current information about the pharmacological basis for the **therapy** of **osteoarthritis**. In addition, the mode of action of the SYSADOAs (SYmptomatic Slow Acting Drugs in **OsteoArthritis**) ademethionine, D-**glucosamine** sulfate, **hyaluronic** acid and oxaceprole obtained from preclinical and clinical studies are described. Until now the **therapy** of **osteoarthritis** still concentrates primarily on the relief of symptoms associated with this disease. At present no evidence has been provided showing that any drug including the SYSADOAs is able to inhibit, decelerate or even reverse morphologically definable cartilage defects in human clinical studies. An analysis of pharmacological results from in vitro and animal experiments reveal that there is still a significant need for more preclinical investigations designed to show whether, and to what extent, the SYSADOAs at clinically relevant concentrations act against the pathogenetically important processes occurring in **osteoarthritic** articular cartilage. Clinical and preclinical studies, however, justify the statement that these agents are clinically effective concerning their abilities as 'SYmptomatic Slow Acting Drugs in **OsteoArthritis**'.

L21 ANSWER 28 OF 40 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 1999316135 MEDLINE
DOCUMENT NUMBER: 99316135 PubMed ID: 10383484
TITLE: Glucosamine sulfate.
AUTHOR: Anonymous
SOURCE: ALTERNATIVE MEDICINE REVIEW, (1999 Jun) 4 (3) 193-5.
Journal code: 9705340. ISSN: 1089-5159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Consumer Health
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990817

AB **Glucosamine** sulfate's role in halting or reversing joint degeneration appears to be directly due to its ability to act as an essential substrate for, and to stimulate the biosynthesis of, the glycosaminoglycans and the **hyaluronic** acid backbone needed for the formation of the proteoglycans found in the structural matrix of joints. Successful **treatment** of **osteoarthritis** must effectively control pain and should slow down or reverse the progression of the degeneration. Biochemical and pharmacological data combined with animal and human studies demonstrate that **glucosamine** sulfate is capable of satisfying both of these criteria.

L21 ANSWER 29 OF 40 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1998429582 MEDLINE
DOCUMENT NUMBER: 98429582 PubMed ID: 9756610
TITLE: Roles of aggrecan, a large chondroitin sulfate proteoglycan, in cartilage structure and function.
AUTHOR: Watanabe H; Yamada Y; Kimata K
CORPORATE SOURCE: Craniofacial Developmental Biology and Regeneration Branch, National Institute of Dental Research, National Institutes of Health, Bethesda MD 20892, USA.. watanabe@yoda.nidr.nih.gov
SOURCE: JOURNAL OF BIOCHEMISTRY, (1998 Oct) 124 (4) 687-93.
Ref: 62
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990121

AB Aggrecan, a large aggregating proteoglycan, is one of the major structural components of cartilage. Its core protein contains three glubular domains and two glycosaminoglycan-attachment domains. These domains play various roles to maintain cartilage structure and function. An N-terminal globular domain binds **hyaluronan** and link protein to form huge aggregates. The **chondroitin sulfate** (CS) chains attach to the CS domain and provide a hydrated, viscous gel that absorbs compressive load. Two autosomal recessive chondrodysplasias, cartilage matrix deficiency (cmd) in

mice and nanomelia in chicken are both caused by aggrecan gene mutations. Cmd homozygotes die shortly after birth, while the heterozygotes are born normal. However, cmd heterozygotes develop late onset of spinal disorder, which suggests aggrecan as a candidate gene predisposing individuals to spinal problems. Nanomelia is a useful model to elucidate intracellular trafficking of proteoglycans. Further studies on aggrecan will lead to prophylaxis and **treatment** of joint destructive diseases such as **osteoarthrosis** and to elucidation of cartilage development, which is essential for skeletal formation.

L21 ANSWER 30 OF 40 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 990261056 JICST-EPlus
TITLE: Relationship Between Joint Markers in Synovial Fluid and Radiographic Findings in Osteoarthritis of the Knee.
AUTHOR: IKEDA K; KATOH Y; ITOH T
TOYOSHIMA H
CORPORATE SOURCE: Tokyo Women's Medical Coll.
Komakidai Clinic
SOURCE: Nippon Riumachi, Kansetsu Geka Gakkai Zasshi (Japanese Journal of Rheumatism and Joint Surgery), (1998) vol. 17, no. 3, pp. 171-178. Journal Code: Y0692A (Fig. 3, Tbl. 2, Ref. 25)
ISSN: 0287-3214
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB Early diagnosis and **treatment** can **prevent** the progression of joint disease, so appropriate examinations are needed that can recognize subtle cartilage degeneration at an early stage and evaluate **treatment** efficacy. In 58 patients with **osteoarthritis**(OA) of the knee, several joint markers were investigated to determine the correlations between their levels and radiographic findings. The levels of **chondroitin** 6-**sulfate**(C6S), **chondroitin** 4-**sulfate** (C4S), and type II procollagen C-peptide(pCOL II-C) were high in the patients, but the C6S/C4S ratio and the **hyaluronic** acid(**HA**) concentration were low compared with the levels in normal controls. A negative correlation was found between radiographic progression and both the C6S level and the C6S/C4S ratio, while a positive correlation was found between radiographic progression and the pCOL II-C level. These results suggest that joint markers, especially C6S, the C6S/C4S ratio, and pCOL II-C, reflect damage to articular cartilage, and that measurement of these markers in joint fluid may be useful for the diagnosis and monitoring of early OA without radiographic abnormalities. Moreover, these parameters could possibly be applied to evaluation of **therapeutic** efficacy. (author abst.)

L21 ANSWER 31 OF 40 MEDLINE on STN
ACCESSION NUMBER: 1998262758 MEDLINE
DOCUMENT NUMBER: 98262758 PubMed ID: 9600024
TITLE: The role of glucosamine sulfate and chondroitin sulfates in the treatment of degenerative joint disease.
AUTHOR: Kelly G S

SOURCE: ALTERNATIVE MEDICINE REVIEW, (1998 Feb) 3 (1) 27-39.
Ref: 34
Journal code: 9705340. ISSN: 1089-5159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Consumer Health
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980605

AB Successful **treatment** of **osteoarthritis** must effectively control pain, and should slow down or reverse progression of the disease. Biochemical and pharmacological data combined with animal and human studies demonstrate **glucosamine** sulfate is capable of satisfying these criteria. **Glucosamine** sulfate's primary biological role in halting or reversing joint degeneration appears to be directly due to its ability to act as an essential substrate for, and to stimulate the biosynthesis of, the glycosaminoglycans and the **hyaluronic** acid backbone needed for the formation of proteoglycans found in the structural matrix of joints. **Chondroitin sulfates** , whether they are absorbed intact or broken into their constituent components, similarly provide additional substrates for the formation of a healthy joint matrix. Evidence also supports the oral administration of **chondroitin sulfates** for joint disease, both as an agent to slowly reduce symptoms and to reduce the need for non-steroidal anti-inflammatory drugs. The combined use of **glucosamine** sulfate and **chondroitin sulfates** in the **treatment** of **degenerative joint disease** has become an extremely popular supplementation protocol in arthritic conditions of the joints. Although **glucosamine** sulfate and **chondroitin sulfates** are often administered together, there is no information available to demonstrate the combination produces better results than **glucosamine** sulfate alone.

L21 ANSWER 32 OF 40 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1997-310614 [28] WPIDS
DOC. NO. CPI: C1997-099986
TITLE: Enzymatic synthesis of hyaluronic acid from UDP derivatives - with regeneration of starting materials from released UDP to reduce feedback inhibition of hyaluronic acid synthase and increase yield.
DERWENT CLASS: B04 D16
INVENTOR(S): DELUCA, C; WONG, C
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST
COUNTRY COUNT: 3
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9720061 | A1 | 19970605 | (199728)* | EN | 50 |
| W: CA JP US | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9720061 | A1 | WO 1995-US15600 | 19951130 |

PRIORITY APPLN. INFO: WO 1995-US15600 19951130
AN 1997-310614 [28] WPIDS
AB WO 9720061 A UPAB: 19970709
An improved method for the enzymatic synthesis of **hyaluronic** acid (**HA**) using **HA** synthase (HAS) to polymerise uridine diphosphate (UDP)-D-glucuronic acid (UDP-GlcA) and UDP-**N-acetyl**-D-**glucosamine** (UDP-GlcNAc) with release of UDP, where the improvement is the simultaneous regeneration of both starting materials from the UDP released, and where the released UDP reduces feedback inhibition of the HAS and thereby enhances the yield of HA.

USE - HA is known for viscosity supplementation in ophthalmic surgery and is used for the **treatment** of **osteoarthritis**.

ADVANTAGE - Reusing the UDP released reduces feedback inhibition of HAS and improves yield of HA. HA of molecular weight about 0.55 million is produced in quantities greater then 30 mg. Dwg.0/14

L21 ANSWER 33 OF 40 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 960946775 JICST-EPlus
TITLE: Intra-articular injection therapy of MR-20S (ulinastatin) for osteoarthritis of the knee joint: Effect on joint markers.
AUTHOR: SAMURA ATSUYOSHI; YAMADA HARUMOTO; YOSHIHARA YASUO; KOBAYASHI TATSUO; KIKUCHI TOSHIYUKI; TANAKA OSAMU
CORPORATE SOURCE: Natl. Def. Med. Coll.
SOURCE: Ensho (Japanese Journal of Inflammation), (1996) vol. 16, no. 5, pp. 357-361. Journal Code: Y0899A (Tbl. 2, Ref. 19)
CODEN: ENSHEE; ISSN: 0389-4290
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB Intra-articular injections of MR-20S (ulinastatin, urinary trypsin inhibitor)were performed for 16 knee joints of 16 patients(6 males, 10 females, average age 65.1±8.2) with **osteoarthritis** (OA). Levels of 7 joint markers in the synovial fluids were measured before and after injection **therapy**. Levels of **chondroitin** 4-**sulfate** (C-4S), 6-sulfate (C-6S) and **hyaluronic** acid(**HA**) were measured using HPLC. Levels of type II procollagen C-peptide (pCOL II-C), MMP-3, TIMP-1 and PMN elastase were measured by EIA Levels of pCOL II-C increased significantly after injections ($p<0.01$). In the patients with C-4S levels of.GEQ.15 nmol/ml or C-6S levels of .GEQ.40 nmol/ml before injection, these chondroitin isomers decreased significantly($p<0.01$). No significant changes of HA, MMP-3, TIMP-1 and PMN elastase levels were observed after injection. The present data suggested that intra-articular injection of MR-20S might affect

the metabolism of cartilage and synovium in OA. (author abst.)

L21 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 16

ACCESSION NUMBER: 1995:498372 BIOSIS
DOCUMENT NUMBER: PREV199598521922
TITLE: Biochemical and pharmacokinetic aspects of oral treatment with chondroitin sulfate.
AUTHOR(S): Conte, A.; Volpi, N. [Reprint author]; Palmieri, L.; Bahous, I.; Ronca, G.
CORPORATE SOURCE: Dep. "Biologia Animale", Via Berengario 14, I-41100 Modena, Italy
SOURCE: Arzneimittel-Forschung, (1995) Vol. 45, No. 8, pp. 918-925.
CODEN: ARZNAD. ISSN: 0004-4172.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 1995
Last Updated on STN: 29 Nov 1995

AB **Chondroitin sulfate** (Condrosulf) was characterized for structure, physicochemical properties and purity. This glycosaminoglycan has a relative molecular mass of about 14,000, a sulfate-to-carboxyl ratio of 0,95 due to the high percentage of monosulfated disaccharides (38% 6-monosulfate and 55% 4-monosulfate) and a low amount of disulfated disaccharides (1.1%) inside the polysaccharide chains. No other glycosaminoglycans were detected in the preparation. **Chondroitin sulfate** was labelled by reduction with sodium 3H-borohydride and administered by oral route in the rat and dog. More than 70% of radioactivity was absorbed and found in urine and tissues. The plasma radioactivity was fractionated by size-exclusion chromatography in three fractions: radioactivity associated with high, intermediate and low molecular mass compounds. The peak value of the concentration of high molecular mass radioactivity compounds in plasma was reached after 1.6 and 2.1 h for the rat and dog, respectively. After 36 h the high molecular mass radioactivity compounds were still present in plasma of dog and rat. After 24 h radioactivity was higher in the intestine, liver kidneys, synovial fluid and cartilage than in other tissues. **Chondroitin sulfate** was orally administered to man (healthy volunteer) in a single daily dose of 0.8 g and in two daily doses of 0.4 g. The results showed that both forms of, administration determined a significant increase of plasma concentration of **chondroitin sulfate** as compared with predose value over a full 24 h period. Elimination constant values and t-max (of the first administration in the case of fractionated dose) were almost the same for the two administrations. Some biochemical parameters (number of leukocytes, proteins, sulfated glycosaminoglycans and **hyaluronic** acid amounts, and N-acetylglucosaminidase activity) of synovial fluid were evaluated in controls and **treated osteoarthritic** subjects. No variations were observed in the patient who did not receive **chondroitin sulfate**. Five days of **chondroitin sulfate** administration led to a significant increase of concentration and molecular mass of **hyaluronan** and a decrease of a lysosomal enzyme, N-acetylglucosaminidase. No significant differences in leukocyte count and protein content were detected.

L21 ANSWER 35 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94212411 EMBASE
DOCUMENT NUMBER: 1994212411
TITLE: Intra-articular hyaluronic acid in osteoarthritis of the knee: An investigation into mechanisms of action.
AUTHOR: Creamer P.; Sharif M.; George E.; Meadows K.; Cushnaghan J.; Shinmei M.; Dieppe P.
CORPORATE SOURCE: Univ. of Bristol Rheumatology Unit, Bristol Royal Infirmary,Bristol BS2 8HW, United Kingdom
SOURCE: Osteoarthritis and Cartilage, (1994) 2/2 (133-140). ISSN: 1063-4584 CODEN: OSCAEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 014 Radiology
020 Gerontology and Geriatrics
031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The objective of this study was to investigate mechanisms of action of intra-articular **hyaluronic** acid in **osteoarthritis** (OA) of the knee. Twelve patients with bilateral knee OA and synovial effusions entered a randomized, single-blind, blind observer study. **Hyaluronic** acid ('Hyalgan', Fidia SpA, Italy) or placebo were given by intra-articular injection weekly for 5 weeks. Assessments included clinical indices and imaging (magnetic resonance imaging (MRI) and 99m Tc bone scanning) before and after the course of injections. In addition, synovial fluid keratan sulfate (KS), **chondroitin sulfate** (CS) and C-propeptide of type II collagen (CPII) were measured. MRI and 99m Tc scanning showed no change in either **treated** or placebo knees over the 6-week study period. A fall in KS levels occurred in **treated** knees compared with placebo (Wilcoxon paired test, P = 0.1), although this did not reach significance perhaps due to small sample numbers). Ten out of 12 **treated** knees showed a fall in KS, compared with four out of 12 placebo knees. CS and CPII levels did not change significantly. Intra-articular injection of **hyaluronic** acid did not result in any improvement in the clinical indices compared to the placebo. In conclusion, assessment of cartilage markers may be of value when studying novel **therapies** in OA. MRI appearances remain remarkably stable over a 6-week period.

L21 ANSWER 36 OF 40 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 93230761 MEDLINE
DOCUMENT NUMBER: 93230761 PubMed ID: 8472428
TITLE: Pharmacologic and clinical aspects of intraarticular injection of hyaluronate.
AUTHOR: Iwata H
CORPORATE SOURCE: Department of Orthopaedic Surgery, Nagoya University School of Medicine, Japan.
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (1993 Apr) (289) 285-91. Ref: 60
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930604
Last Updated on STN: 19930604
Entered Medline: 19930520

AB **Hyaluronate** (**HA**) is linear unbranched polysaccharide consisting of repeating disaccharide units of (1-4)-D-glucuronic acid-beta-(1-3)-D-N-**acetylglucosamine**. Extensive research has been conducted on HA, a major component of connective tissue. Hyaluronate, molecular weight 80 x 10(4)d, is available for the intraarticular injective **treatment** of **osteoarthrosis** of the knee and periarthritis of the shoulder. **Hyaluronate** relieves pain and **has** metabolic effects on articular cartilage, synovial tissue, and synovial fluid. Hyaluronate is a safe and effective **treatment** for patients with **osteoarthrosis** of the knee and periarthritis of the shoulder.

L21 ANSWER 37 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 87231937 EMBASE
DOCUMENT NUMBER: 1987231937
TITLE: Combination of glycosaminoglycan and acetylsalicylic acid in knee osteoarthrosis.
AUTHOR: Kerzberg E.M.; Roldan E.J.A.; Castelli G.; Huberman E.D.
CORPORATE SOURCE: Department of Medicine, Division 'C', J.M. Ramos Mejia Hospital, Buenos Aires, Argentina
SOURCE: Scandinavian Journal of Rheumatology, (1987) 16/5 (377-380).
ISSN: 0300-9742 CODEN: SJRHAT
COUNTRY: Sweden
DOCUMENT TYPE: Journal
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English

AB The initial biochemical alteration in **osteoarthrosis** appears to be a reduction of the proteoglycan content of the articular cartilage, due to a greatly increased catabolism. The administration of exogenous glycosaminoglycans (GAG), the non-proteic moiety of the proteoglycan molecule, inhibits the enzymic degradation of both proteoglycans and collagen. There is clinical evidence that some GAG, such as **chondroitin sulphates** (long chains of **hyaluronic** acids linked to N-acetylgalactosamides sulphated in C4 and C6 position) improve the symptom picture in patients with **osteoarthrosis**. So far, no serious adverse effects due to the prolonged administration of GAG in man have been reported. We are investigating the clinical action of GAG associated with a standard **treatment** with acetylsalicylic acid (aas) in patients with **osteoarthrosis** of the knee joint, to study its possible synergistic effect.

L21 ANSWER 38 OF 40 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 85218584 MEDLINE
DOCUMENT NUMBER: 85218584 PubMed ID: 4001876

TITLE: Effects of sodium diclofenac on glycosaminoglycan metabolism in experimental osteoarthritis in rabbits.
AUTHOR: Eronen I; Videman T
SOURCE: SCANDINAVIAN JOURNAL OF RHEUMATOLOGY, (1985) 14 (1) 37-42.
Journal code: 0321213. ISSN: 0300-9742.
Report No.: NASA-85218584.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850703

AB The effect of diclofenac sodium (DS) on the metabolism of glycosaminoglycans (GAG) was studied in rabbits during the development of osteoarthritis of the knee induced by immobilization. Contents of **hexosamines**, uronic acid and sulphate-derived 35S-radioactivity in separated GAGs were determined. DS was given to 6 immobilized rabbits for 17 days at a dose of 1.5 mg/kg through a stomach tube. The controls consisted of 8 immobilized rabbits without medication and of 21 non-immobilized rabbits, 6 of which received DS for 17 days. DS did not inhibit in vivo metabolism of sulphated GAGs, according to measurements of [35S]-sulphate incorporation. Healthy rabbits given DS showed only marginal changes of GAG content in joint tissues. DS did not prevent the loss of GAG from the weight-bearing cartilages of the immobilized knees, but caused a further loss of **chondroitin sulphates** accompanied by an increased amount of **hyaluronic** acid in the tissues. DS **prevented** accumulation of the GAGs, which normally occurs during development of **osteoarthritis** in tissues of the tibial margin and in collateral ligaments. The findings indicate that the effect of DS on the GAG metabolism in connective tissues is somewhat different from that with other non-steroidal anti-inflammatory agents.

L21 ANSWER 39 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 83001411 EMBASE
DOCUMENT NUMBER: 1983001411
TITLE: Biosynthesis of proteoglycan in vitro by cartilage from human osteochondrophytic spurs.
AUTHOR: Malemud C.J.; Goldberg V.M.; Moskowitz R.W.; et al.
CORPORATE SOURCE: Cartilage Res. Lab., Dep. Med., Div. Rheumatol., Case West. Reserve Univ., Cleveland, OH 44106, United States
SOURCE: Biochemical Journal, (1982) 206/2 (329-341).
CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

AB Proteoglycan biosynthesis by human osteochondrophytic spurs (osteophytes) obtained from **osteoarthritic** femoral heads at the time of surgical joint replacement was studied under defined culture conditions in vitro. Osteophytes were primarily present in two anatomic locations, marginal and epi-articular. Minced tissue

slices were incubated in the presence of [35S]sulphate or [14C] **glucosamine**. Osteophytes incorporated both labelled precursors into proteoglycan, which was subsequently characterized by CsCl-isopycnic-density-gradient ultracentrifugation and chromatography on Sepharose CL-2B. The material extracted with 0.5 M-guanidinium chloride showed 78.1% of [35S]sulphate in the A1 fraction after centrifugation. Only 23.0% of the [35S]sulphate in this A1 fraction was eluted in the void volume of Sepharose CL-2B under associative conditions. About 60-80% of the [35S]sulphate in the tissue 4 M-guanidinium chloride extract was associated with monomeric proteoglycan (fraction D1). The average partition coefficient (K(av)) of the proteoglycan monomer on Sepharose CL-2B was 0.28-0.33. Approx. 12.4% of this monomer formed stable aggregates with high-molecular-weight **hyaluronic** acid in vitro. Sepharose CL-2B chromatography of fractions with lower buoyant densities (fractions D2-D4) demonstrated elution profiles on Sepharose CL-2B substantially different than that of fraction D1, indicative of the polydisperse nature of the newly synthesized proteoglycan. Analysis of the composition and chain size of the glycosaminoglycans showed the following: preferential elution of both [35S]sulphate and[14C]**glucosamine** in the 0.5 M-LiCl fraction on DEAE-cellulose; the predominant sulphated glycosaminoglycan was **chondroitin** 6-**sulphate** (60-70%), with 9-11% keratan sulphate in the monomer proteoglycan; K(av), values of 0.38 on Sephadex G-200 and 0.48 on Sepharose CL-6B were obtained with papain-digested and NaBH4-**treated** D1 monomer respectively. A comparison of the synthetic with endogenous glycosaminoglycans indicated similar types. These studies indicated that human osteophytes synthesized in vitro sulphated proteoglycans with some characteristics similar to those of mature human articular cartilage, notably in the size of their proteoglycan monomer and predominance of **chondroitin** 6-**sulphate**. They differed from articular cartilage primarily in the lack of substantial quantities of keratan sulphate and aggregation properties associated with monomer interaction with **hyaluronic** acid.

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ACCESSION NUMBER: 80239656 EMBASE
DOCUMENT NUMBER: 1980239656
TITLE: Dibutyryl cyclic AMP affects hyaluronate synthesis and macromolecular organization in normal adult articular cartilage in vitro.
AUTHOR: Stack M.T.; Brandt K.D.
CORPORATE SOURCE: Rheumatol. Div., Indiana Univ. Sch. Med., Indianapolis, Ind. 46223, United States
SOURCE: Biochimica et Biophysica Acta, (1980) 631/2 (264-277).
CODEN: BBACAQ
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

AB When normal adult dog articular cartilage was cultured in the presence of dibutyryl cyclic AMP a higher proportion than normal of newly synthesized 35S-labeled glycosaminoglycans was released from the tissue into the culture medium, although their net synthesis was

not affected. In conjunction with this release of sulfated glycosaminoglycans, 24 times more [3H]**glucosamine**-labeled **hyaluronic** acid was released from the cartilage into the medium, and net hyaluronate synthesis was enhanced 3-fold. Virtually all of the newly synthesized **hyaluronic** acid in the medium was associated with proteoglycans. The proteoglycans in the medium of the dibutyryl cyclic AMP **treated** cultures were normal in hydrodynamic size and interacted normally with **hyaluronic** acid to form large aggregates. These results suggest that the increase in hyaluronate synthesis caused by dibutyryl cyclic AMP may have destabilized the interaction of proteoglycans with the collagen meshwork of the cartilage. The changes seen in normal adult articular cartilage after incubation with dibutyryl cyclic AMP, therefore, are similar to those which are observed in cartilage of **osteo-arthritic** joints.

(FILE 'MEDLINE' ENTERED AT 08:59:41 ON 13 FEB 2004)

L22 275 SEA FILE=MEDLINE ABB=ON PLU=ON (HYALURONIC ACID AND OSTEOARTHRITIS)/CT

L23 21 SEA FILE=MEDLINE ABB=ON PLU=ON L22 AND (HEXOSAMINES OR HEXOSES OR CHONDROITIN SULFATES)/CT

L24 2 SEA FILE=MEDLINE ABB=ON PLU=ON L23 AND (THERAPY OR THERAPEUTIC USE)/CT

L24 ANSWER 1 OF 2 MEDLINE on STN

AN 2001237407 MEDLINE

TI The increasing need for nonoperative treatment of patients with osteoarthritis.

AU Buckwalter J A; Stanish W D; Rosier R N; Schenck R C Jr; Dennis D A; Coutts R D

SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (2001 Apr) (385) 36-45. Ref: 91
Journal code: 0075674. ISSN: 0009-921X.

AB Osteoarthritis affects more patients than almost any other musculoskeletal disorder. The number of patients suffering joint pain and stiffness as a result of this disease will increase rapidly in the next decade. Although operative treatments of patients with osteoarthritis will continue to improve and the number of operative procedures will increase slightly in the next decade, only a small fraction of the patients with osteoarthritis will require operative procedures. The most pressing healthcare need for the majority of patients with osteoarthritis is nonoperative care that helps relieve symptoms and improve function, and in some instances slows progression. In rare instances, the symptoms of osteoarthritis improve spontaneously, but most patients need nonoperative care for decades. Orthopaedists need to improve their ability to provide nonoperative care for patients with osteoarthritis. They should be skilled in the early diagnosis of osteoarthritis and in the use of current common nonoperative treatments including patient education, activity modification, shoe modifications, braces, oral analgesics, oral nonsteroidal antiinflammatory medications, oral dietary supplements, and intraarticular injections. Furthermore, orthopaedists should be prepared to incorporate new nonoperative treatments for patients with osteoarthritis into their practice.

L24 ANSWER 2 OF 2 MEDLINE on STN

AN 1999136440 MEDLINE

TI Will we be able to repair osteoarthritic joints? New drugs and

surgical techniques for cartilage problems.
AU Almekinders L C
SO NORTH CAROLINA MEDICAL JOURNAL, (1999 Jan-Feb) 60 (1) 46-8.
Journal code: 2984805R. ISSN: 0029-2559.

FILE 'HOME' ENTERED AT 09:00:49 ON 13 FEB 2004